Vol. 5 No. 2. December, 1945

ANNALS OF THE RHEUMATIC DISEASES

EDITORIAL COMMITTEE

C. W. BUCKLEY

NORMAN CAPENER
W. S. C. COPEMAN
G. D. KERSLEY
PHILIP S. HENCH (U.S.A.)
A. G. TIMBRELL FISHER
MERVYN H. GORDON
C. BRUCE PERRY
LORING T. SWAIM (U.S.A.)

EDITOR OF THE *British Medical Journal*

APPOINTED BY THE
BRITISH MEDICAL ASSOCIATION AND THE EMPIRE RHEUMATISM COUNCIL

LIBRARY OF THE MEDICAL SOCIETY OF THE COUNTY OF KINGS
JUN 24 1946
AND ACADEMY OF MEDICINE OF BROOKLYN
BEDFORD AVENUE
BROOKLYN, N. Y.

CONTENTS

LONDON
BRITISH MEDICAL ASSOCIATION
TAVISTOCK SQUARE, W.C.1

YEARLY SUBSCRIPTION (4 NUMBERS) 25/- U.S.A. $6.00 SINGLE NUMBER 7/6

NOTICE TO SUBSCRIBERS

Subscriptions are payable to the British Medical Association. Address: British Medical Association House, Tavistock Square, London, W.C.1.

NOTICE TO CONTRIBUTORS

Papers submitted to this Journal are accepted on the understanding that they have not been and will not be published in any other journal, and are subject to editorial revision. All papers and other editorial communications should be addressed to Dr. C. W. Buckley, Bentley Cottage, Ashbourne, Derbyshire.

The author of an original article should make adequate references to previous work on his chosen subject.

A full summary of his observations and conclusions must be given.

A paper describing a single case will not be accepted unless the case is sufficiently rare, or shows important features not previously described, or has been made a subject of special observation or experiment.

Articles must be as concise as possible and be typewritten on one side of the paper only, with double spacing and a margin of not less than 1¼ inches. Only recognized abbreviations should be used. Graphs, charts, tables, and legends for them should be presented on separate sheets and not included in the text. When half-tone reproduction of x-ray illustrations is required, the author is advised to send the original film unless he wishes to bring out special points in a print of his own choice. Photographs and photomicrographs should be printed on glossy paper, should be larger than the size desired for reproduction, and, if transmitted through the post in a tube, should be rolled with the picture outside. With the exception of letters and numbers, which should be lightly written in pencil, everything that is to appear in the reproduction of a graph or chart should be carefully drawn in black ink on tracing linen, or Bristol board, or stout, smooth, white paper.

References should be arranged according to the Harvard system. In the text, the year of publication must follow the author's name, more than one paper in any one year being indicated by a small letter (*a*, *b*, *c*) after the date. No numbering of references is necessary. At the end of the contribution references are arranged in the alphabetical order of the author's names. The reference details are given as follows: Author's name and initials, year of publication (in parentheses), title of periodical (in italics, abbreviated according to the *World List of Scientific Periodicals*), volume number (bold type, Arabic numerals), and first page number (ordinary type, Arabic numerals), thus:

Cowan, J. (1929). *Quart. J. Med.*, **22**, 237.

When a book is referred to, the full title, publisher, the place and year of publication, edition and page number should be given.

Contributors will receive one proof in page, but it is assumed that all but verbal corrections have been made in the original manuscript; an allowance at the rate of ten shillings per sheet of sixteen pages is made for alterations in the proof (printer's errors excepted), and contributors will be responsible for any excess.

Fifty free reprints of articles will, if desired, be given to contributors. A limited number of additional reprints at cost price can be supplied if application is made when returning proofs. An estimate of costs will be given on application to the Publishing Manager, British Medical Association.

Papers which have been published become the property of this Journal, and permission to republish must be obtained from the Editors.

Application for Advertisement space should be addressed to the Advertisement Manager, British Medical Association, Tavistock Square, London, W.C.1.

ANATOMY AND PHYSIOLOGY OF DIARTHRODIAL JOINTS

BY

D. V. DAVIES

School of Anatomy, Cambridge

It is proposed to deal only with the freely moving diarthrodial joint with a synovial cavity, omitting many points of interest about the gross anatomy and the mechanics of joints.

The several components of the diarthrodial joint are derived from mesoderm. The joint cavity is developed by liquefaction of the mesenchymal tissue which at first separates the chondrified skeletal elements. The perichondrium (later periosteum) is continued over this cavity as the capsule, while the lining of the cavity presents, on the ends of the bones, the articular cartilage and, on the capsule, the synovial membrane. In some cases, such as the knee and temporo-mandibular joint, liquefaction occurs in two regions in close proximity, the intervening mesenchyme forming the joint disk or meniscus. The capsule, like the periosteum or perichondrium, is composed of tough, inelastic, white fibrous tissue with marked powers of resistance to disease and relatively low powers of repair. The synovial membrane, on the other hand, is a thin, soft, freely movable, elastic membrane, richly supplied with pain fibres, with an abundant blood supply, good powers of repair and well-marked phagocytic properties.

Articular Cartilage

The articular cartilage is admirably adapted to its purpose. It is so smooth that when lubricated with synovia the friction between the surfaces is reduced to a minimum; it is so elastic that it prevents any jarring of the bones upon one another. It is devoid of sensation so that the movements of the joint, during which the cartilages are subjected to a good deal of pressure by the contraction of muscle and the tension of the ligaments, take place without pain. Finally, it is avascular. "Throughout the life cycle cartilage lives, grows, and decays without a blood supply, without a demonstrable nerve supply" (Harris, 1933). Subjacent to the articular cartilage and separating it from the underlying vascular bone is a zone of calcified cartilage. This increases in depth with age. The articular cartilage when traced towards the joint cavity shows a series of graduated senescent changes likened by Harris (1933) to those seen in the epidermis. Bordering on the calcified cartilage is a zone of proliferation where the cells are frequently arranged in groups of twos and fours, though cells in the act of division are rarely seen. In young bone this zone is continuous at the articular margins with the zone of proliferating cartilage in the epiphyseal disk, these together constituting the mitotic annulus of Harris (1933) (Fig. 1).

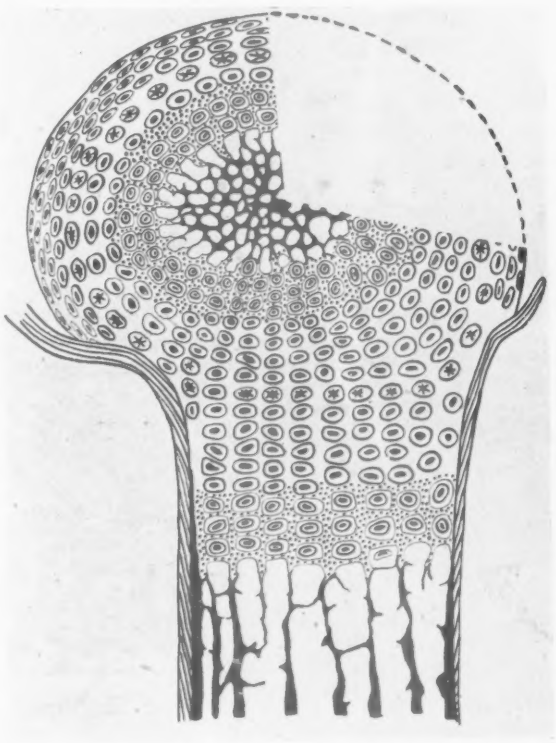

FIG. 1.—Diagram showing the zone of mitoses in articular and epiphyseal cartilages. The cells in this zone have their nuclei shown in the form of asters. (Harris: *Bone Growth in Health and Disease*, 1933, Fig. 121.)

In the immature animal the normal mechanism of division in the articular cartilage is by mitosis, possibly giving way with age to amitotic division (Elliott, 1936). When traced towards the articular surface the cells derived from this zone of proliferation become flattened and arranged tangentially, gradually losing their staining reaction and shrinking. They reach the articular surface as a sheet of senescent and dead cells to be removed by the constant wear and tear which accompanies joint movements. This senescence and death of cartilage cells has been disregarded in all studies concerning

the metabolism of articular cartilage. The cell content of articular cartilage decreases with age while the proportion of matrix is correspondingly increased. Rosenthal and his colleagues (1941) estimate that the cell content of bovine articular cartilage decreases by two-thirds from youth to adolescence and by three-quarters from youth to old age.

Even in its deepest layers the metabolic requirements of articular cartilage can be met from substances in the synovial fluid. The respiratory rate of articular cartilage per unit of weight is low as compared with other tissues. The high proportion of matrix accounts for this, so that the glycolytic power per cell is said to be the same as that of other tissues (Bywaters, 1937). The metabolic activity of the cartilage cell is further said to decrease appreciably with age, according to Rosenthal and his colleagues (1941) by 60% from young to adult in cattle. Whether this is explicable on the basis of the changing proportions of proliferating to senescent cells has not been considered.

The reparative powers of articular cartilage are feeble. Lesions confined to the articular cartilage over the weight-bearing surfaces show little or no evidence of repair. At the articular margins repair

FIG. 2.—Section through the articular cartilage on the head of the radius showing the repair of a six weeks' old fracture. The proliferation of the connective tissue from the marrow spaces to fill the defect in the articular cartilage is seen. × 41.

may be effected by the ingrowth of synovial tissue, which may become transformed into an imperfect fibrous cartilage. Lesions extending through the articular cartilage into the underlying vascular bone and marrow spaces are repaired by proliferation of the connective tissue from the latter, the deeper layers of which may ossify while the most superficial layers may yield a mixture of fibrous tissue and fibrocartilage at the articular surface (Graville *et al.*, 1932; Fisher, 1923). This is also the response in fractures involving articular surfaces (Fig. 2).

Apposition of articular surfaces is essential for the preservation of the normal structure and function of the articular cartilage. Loss of apposition

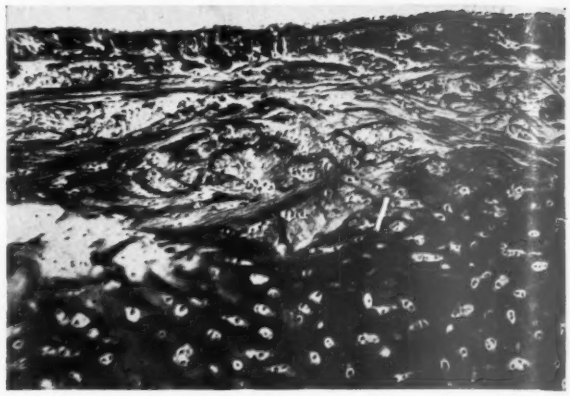

FIG. 3.—Section of the detached fragment from a typical case of osteochondritis dissecans, showing the transformation of the articular cartilage into fibrous tissue. × 66.

leads to a degeneration of the cartilage and its transformation into fibrous tissue. Such a transformation into fibrous tissue is seen in the acetabulum in cases of congenital dislocation of the hip, and in the cartilage covering loose bodies detached from the articular surfaces, as in osteochondritis dissecans (Fig. 3).

Articular cartilage possesses considerable resistance to autolysis both *in vivo* and *in vitro*. It also resists the action of various enzymes and toxins which occur in normal and abnormal synovial fluids.

Intra-articular disks

There has been much speculation in the past as to the morphological and functional value of intra-articular disks or menisci. The constancy of their occurrence and distribution in the mammals is worthy of note. A washer-like action, minimizing the incongruity at the joint surfaces, is hardly justified by their distribution. They are found in the temporo-mandibular joints of practically all mammals, irrespective of the configuration of the joint surfaces. They are even present in the carnivores, in which the articular surfaces are transverse concentric cylinders, accurately adapted one to the other and allowing uni-axial movement. A buffer or shock-absorbing function fails to receive support from their distribution. MacConaill (1932) supposes that they act in the nature of Michel pads, helping to maintain a film of lubricant between the articular surfaces. In most positions of the joint they maintain rather than decrease the incongruity between the articular surfaces, thus creating a wedge-shaped interval, pointing in the direction of motion, through which synovial fluid is continuously fed on to the articulating surfaces.

Structurally they consist not of pure fibrocartilage but of a mixture of cartilage embedded in a much larger mass of dense fibrous tissue. Their removal is said to be followed by a regeneration of fibrous pads from the synovial membrane (Bruce and Walmsley, 1937). Whether this regeneration constantly occurs in all animals and irrespective of age remains unsettled.

Synovial Membrane

The synovial membrane covers all the joint surfaces except the cartilage-covered weight-bearing areas. It affords an investment to any tendons or ligaments passing through the joint, covers the edges of the articular cartilage, with which it is firmly adherent, and terminates gradually by shading off into the superficial layer of the cartilage without sharp demarcation. Normally it is very thin and its internal surface is furnished with a variable number of delicate villi and folds, such as the alar folds in the knee-joint, and at the articular margin delicate, frequently overlapping, vascular fringes (Figs. 7 and 8). Occasional cord-like bridges are seen at its reflections from bone to capsule.

The surface of the membrane is relatively cellular,

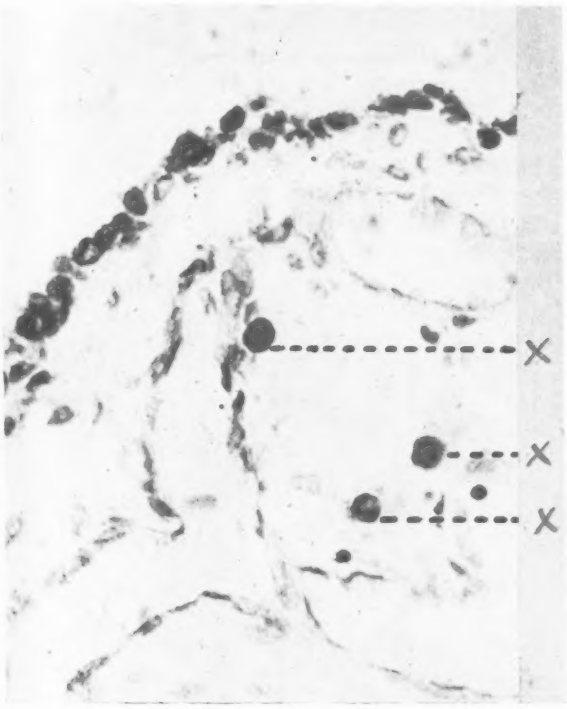

FIG. 4.—Section of the synovial membrane from the ankle-joint of an ox to show the perivascular distribution of the metachromatically stained cells (x). Stained with polychrome methylene blue. × 375.

some portions being richer in cells than others. The cells vary much in size and are generally irregularly branched, the surface of the membrane between the cells, and sometimes over them, being formed by a homogeneous eosinophilic ground substance or by collagenous fibres. No cells with the morphological characters and staining reactions of goblet cells are seen in the synovial membrane. Cells staining metachromatically with toluidine blue or thionin do occur in the deeper layers. These have been characterized as mucin-secreting but must be considered as mast cells on account of their characters and perivascular distribution. They are never seen actually at the synovial surface (Davies, 1943) (Fig. 4).

Velpeau (quoted by Todd, 1836), and more recently Key (1928), ascribed much importance to the connective tissue underlying the synovial membrane. Its quantity and quality determines the mobility of the synovial membrane. At the articular margins and lining the ligaments it consists of dense collagenous tissue, restricting independent mobility of the synovial membrane. Elsewhere the underlying tissue is of a loose areolar texture, allowing free movement of the synovial membrane. In most joints there are localized accumulations of fat in various regions in this tissue forming distinct pads, erroneously regarded by Clopton Havers (Todd, 1836) as mucilaginous glands. They fill up the spaces between the bones and between the bones and ligaments in the movements of the joints. According to MacConaill

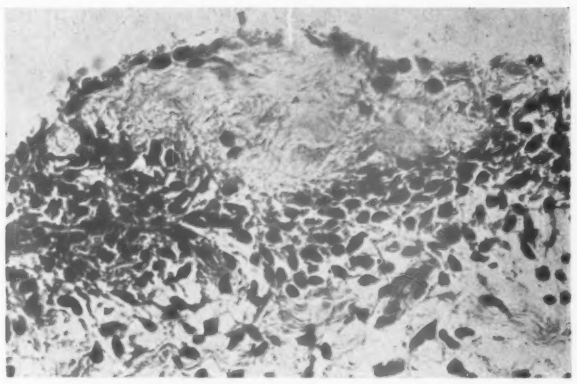

FIG. 5.—Section of the synovial membrane from a human knee-joint, showing the incorporation into the membrane of a deposit of fibrin from the joint. × 300.

(1932) they affect the distribution of the synovial fluid within the joint. The more mobile areas of synovial membrane are provided with an abundance of elastic fibres, often forming one or more distinct elastic laminae. This prevents the membrane being nipped between the articular surface during movement. Villi are devoid of elastic fibres except those in association with the blood vessels. Elastic fibres are sparse where the synovial membrane is firmly adherent to the underlying tissues (Davies, 1946b).

The extent of the synovial membrane in the various joints, and its relation to the area of articular cartilage, is clearly important in connexion with the nutritive functions of the joint. Despite this, comparative figures are not available. Isolated estimates show that whereas in the human knee-joint the area of the synovial membrane is almost double that of the cartilage, in the ankle the proportion is nearer unity (Davies, 1946b).

Much confusion exists as to the nature of the synovial lining. A distinction is frequently drawn between the synovial membrane and the lining of other serous cavities, such as the pleura or peritoneum. Recently the synovial lining has been defined as modified connective tissue. There is little morphological resemblance between the flattened connective tissue lining of false joints and the

lining layer of true joints (Davies, 1946b). The cells lining the synovial membrane differ from fibroblasts on culture in their ability to lyse fibrin and to secrete a mucin-like substance (Vaubel, 1933a and b). Nor is there much morphological resemblance between the lining of the synovial membrane and that of serous cavities like the pleura or peritoneum. Both, however, exhibit similar reactions to irritation. Key (1928) claims that, following synoviectomy, the lining is reformed by metaplasia of the underlying connective tissue, but there is nothing to show that the newly formed lining preserves the peculiar characters of synovial cells or that the fluid within the joint is not modified by this procedure. In contrast with this is the process of incorporation of fibrin deposits into the synovial membrane by an overgrowth of synovial cells from the periphery of such a deposit, and its subsequent organization (Fig. 5).

Blood Supply and Lymphatic Drainage

The joint, like the periosteum, is supplied by numerous freely anastomosing blood vessels from the main arteries in the neighbourhood. Free

FIG. 6.—Photograph of a cleared specimen of synovial membrane and articular cartilage from the metacarpo-phalangeal joint of an ox, showing the vascular loops at the articular margin. The blood vessels have been injected with India ink. × 27½.

communication exists between the articular blood vessels and those of the adjoining epiphyses. In the synovial membrane the capillaries form a finely meshed network so close to the joint surface that some observers have thought that some of the capillaries may be naked at this surface. The blood vessels advance a short distance upon the non-weight-bearing regions of the articular cartilage, forming the looped anastomoses of the circulus articuli vasculosus of William Hunter (1743) (Fig. 6). In the villi and fringes they form delicate tufts supplied by one or more central arterioles (Figs. 7 and 8). The richness and superficial position of the synovial capillaries account for the frequency of haemorrhages into the synovial cavity. Simple puncture is almost invariably followed by some extravasation of red blood cells into the synovial fluid, while small extravasations of red cells, not recognizable clinically, accompany almost all traumatic lesions in the vicinity of the joint. Simple bruising over a joint is frequently associated with some extravasation of blood into the fluid. No comparison of the blood supply of joint tissues per gramme per minute with that of other tissues and

FIG. 7.—Photograph of the synovial folds and fringes from the metacarpo-phalangeal joint of an ox. The blood vessels have been injected with India ink and the specimen cleared. × 22.

FIG. 8.—High-power view of one of the fringes from the preceding specimen. × 84.

organs is available. The early liberation of nitrogen into the joint in decompression sickness suggests that the capillaries are near the surface and permeable.

The lymphatic vessels of the synovial membrane are neither as numerous nor as superficial as the blood vessels. Unlike other serous cavities it has generally been considered that no direct communication exists between the cavity of the joint and the lumen of its lymphatics. A single widely-meshed lymphatic plexus lies in the synovial membrane. Within the meshes are numerous blindly ending vessels often exhibiting terminal lacuniform enlargements directed towards the surface of the membrane. From this plexus the main vessels pass in groups of twos and threes along the blood vessels towards the flexor aspect of the limb, and communicate freely with the lymphatic plexus on the periosteum (Fig. 9). Few valves occur in the synovial lymphatics but these are frequent in the periosteal vessels (Davies, 1946a).

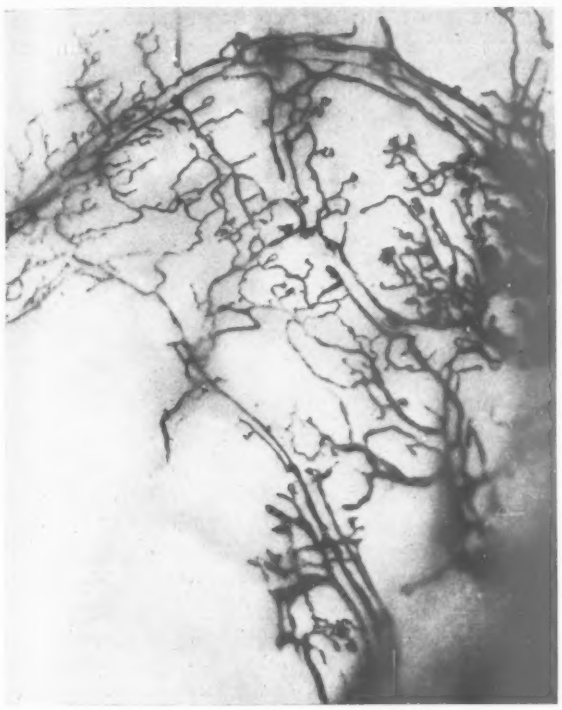

FIG. 9.—Cleared specimen of the synovial membrane from the metatarso-phalangeal joint of an ox, showing the lymphatic vessels. The lymphatics have been injected with India ink. × 10.

Synovial Membrane Nerve Supply

The nerves to the synovial membrane, both medullated and non-medullated, are partly destined for the blood vessels and for the most part accompany them in their course. The vasomotor nerves, presumably of sympathetic origin, continue along the blood vessels. Many of the remainder terminate as free nerve endings in the more superficial parts of the membrane. These presumably subserve pain sensations to which the synovial membrane is markedly susceptible. Other nerve endings, variously described as of the Ruffini, Golgi-Mazzoni, looped or knotted type, are possibly concerned with sensations such as tension, pressure, or proprioception. Gardner (1942) states that in the mouse the encapsulated nerve endings in the synovial membrane show a distribution which would indicate that they may be stimulated by pressure produced by flexion of the joint. Little is known concerning the extent to which the synovial membrane responds to such stimuli. In an isolated case where the synovial membrane of the knee-joint was exposed and opened under local anaesthesia no evidence of any sensation of pressure touch was found in the synovial membrane away from the area of the infiltration and incision. Tension applied from the edge of the incision of the membrane was appreciated, but its localization was particularly inaccurate. Sensitivity to pain was tested by a sharp needle. This sensation was acute but its localization again failed to be very accurate, except that the side of the joint stimulated was always appreciated correctly.

The physiological co-ordination which exists between the joint and the overlying tissues is summed up in Hilton's Law (John Hilton, 1863). "The same trunks of nerves whose branches supply the groups of muscles moving a joint also furnish a distribution of nerves to the skin over the insertions of the same muscles and—what at this moment more especially merits our attention—the interior of the joint receives its nerves from the same source."

Exchange of Substances across the Synovial Barrier

Solutions and particles of small molecular dimensions pass rapidly in either direction across the synovial barrier, mainly through the blood capillary bed. The lymphatic system plays a minor part in their absorption; the role of the synovial membrane in this process is probably purely passive though there are some anomalies as yet unexplained by the known laws of osmosis and diffusion. Colloidal particles, including proteins, reach the joint more slowly and their removal is proportionately slow. The synovial cells and phagocytes play an important

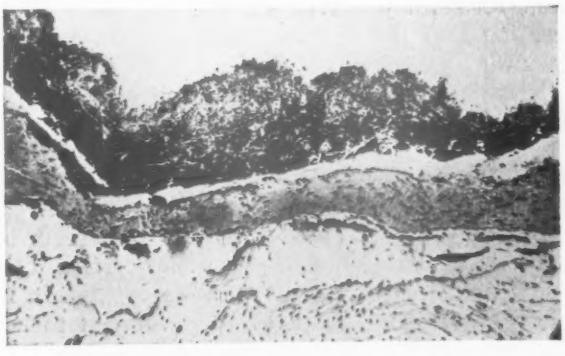

FIG. 10.—Section of the synovial membrane from a human knee-joint, to show the accumulation of haemosiderin. The joint contained a single osteocartilaginous loose body. × 55.

part in their transfer across the synovial barrier. Particulate matter of 100μ upwards passes slowly into the subsynovial tissues and is deposited there. Haemosiderin collects there in large quantities following haemorrhage into the joint cavity (Fig. 10). In the removal of particulate matter from the joint the synovial cells and phagocytes of the synovial membrane play an important part. Movement affects the rate of absorption, particularly of small colloidal material. Its effect on the rate of absorption of solutions is less noticeable on account of their very rapid removal even when the joint is immobilized (Adkins and Davies, 1940). Acute inflammation increases the rate of exchange across the synovial barrier; the effects of chronic inflammation seem variable.

Investigations of the absorption from the joint cavity have been mainly confined to animals and, almost without exception, to the knee-joint. It is possible that the rate of transference across the synovial barrier differs from joint to joint in the same animal.

Synovial Fluid

The synovial fluid differs in its physical, chemical, and cytological characters from joint to joint. The synovial fluid is a viscid, yellowish or colourless, glairy fluid. Its physical characters vary from animal to animal and from joint to joint in the same animal. Its volume bears no close relation to the size or capacity of the joint, though it is moderately constant for any particular joint. The human knee-joint generally contains a small volume (0·2 to 0·3 c.cm.) of pale straw-coloured fluid, while the smaller knee-joint of sheep or dog contains an equal volume of highly viscous colourless fluid. In the ox the knee-joint contains about 10 c.cm. of fluid, while the smaller ankle-joint has on an average 25 c.cm., and sometimes considerably more. In the ankle of the ox the fluid is pale yellow and has a relative viscosity of about 5 at 20° C., while in the atlanto-occipital or atlanto-axial joints of the same animal the fluid is generally of a deep yellow colour and sets to a gel at 20° C. In any particular joint there is no constant relation between the volume and the viscosity of the fluid. Serial changes in its physical characters are seen in the costo-vertebral joints of the ox, the volume decreasing and the viscosity increasing on passing backwards (Davies, 1944).

Knowledge of the composition of the synovial fluid is essential to the understanding of its nature. The most reliable and complete analyses are provided by Bauer and his colleagues (1940); all previous examinations have been fragmentary. Of the blood proteins, albumin and globulin occur in the fluid in considerably lower concentration than in the serum, with a preponderance of albumin in the proportion of about 4 : 1, in contrast to the 1 : 1 ratio found in the serum. There is no fibrinogen in the synovial fluid, hence it does not clot on standing, but the mucin may be precipitated in a sac-like fashion, presumably due to *p*H changes.

Non-electrolytes—urea, uric and amino acids—are in approximately the same concentration in the synovial fluid as in the serum, suggesting free diffusion of these substances across the barrier of synovial membrane. The concentration of glucose in the fluid is generally less than that in the blood, possibly connected with a consumption of glucose within the joint. Any appreciable increase in the cell content of the synovial fluid is associated with a fall in the glucose content.

The distribution of electrolytes in the synovial fluid is in accord with the Donnan equilibrium theory. There is a higher concentration of chlorides and bicarbonates, a similar concentration of inorganic phosphate, and a lower concentration of sodium, potassium, and magnesium. Compared with blood the calcium concentration is high. Part of this calcium is bound to the mucin and the concentration of calcium in the fluid is proportionate to the mucin content and viscosity (Davies, 1946b). A typical example from an ox is:

Source of fluid	Relative viscosity at 20° C.	Calcium in mgm./100 c.cm.
Atlanto-occipital joint	Set into a gel.	10·6
Radio-carpal joint	Approximately 2,000.	7·8
Ankle	7	6·9

Any condition causing increased permeability of the synovial membrane leads to increases in the calcium content of the synovial fluid without necessarily yielding parallel increase in the mucin and the viscosity. Such disproportionate increase in the calcium is seen following aspiration of the fluid from the normal joint in the ox. More data concerning the variations in composition of synovial fluid from joint to joint are required.

The viscous polysaccharide of the synovial mucin has recently been isolated by Meyer, Smyth and Dawson (1939). It is a sulphate-free compound termed hyaluronic acid and differs in respect to its sulphate-free nature from the sulphate-containing mucins found in cartilage and gastric secretions (chondritin and mucoitin sulphuric acids). Hyaluronic acid is also found in the viscous components of Wharton's jelly of the umbilical cord, in the vitreous of the eye, and in connective tissue. It is a substance of high-molecular weight, does not dialyse through colloidin membranes, and is non-antigenic. It does not stain metachromatically with such dyes as toluidine blue or thionin, as do the sulphate-containing mucins. Its viscosity is destroyed or decreased by many agents. Among these are vitamin C, which is consequently not found in synovial fluid (Mann, 1940), and an enzyme, hyaluronidase, which is found in testicular extracts and in semen. A similar enzyme is also produced by certain bacteria.

Cell Content and Cytology

Observations on the cell content and cytology of normal human synovial fluid are few and confined to the knee-joint. The largest series is that of Coggeshall, Warren, and Bauer (1940), involving 29 observations from a series of 16 cases, ranging from 32 to 80 years of age. The average nucleated cell count was 63 per c.mm. with a range of 13 to 180 cells per c.mm. The fluid was obtained immediately post mortem; the subjects mainly suffered from chronic diseases and had been confined to bed for some time before death. The following limited observations from cases suffering sudden death by accident and having no evidence of articular disease indicate that these values are probably too low for subjects maintaining full use of their joints:

Case No.	Sex	Age	Joint	Nucleated cells per c.mm.	Red blood cells per c.mm.
1	M	25	Right elbow	420	0
1	M	25	,, knee	481	186
2	M	56	Left elbow	234	2,000
3	F	12	,, knee	286	4,000
4	M	23	Right ankle	80	21
4	M	23	Left knee	152	26
4	M	23	Right knee	146	39

In this connexion studies on the cell content of animal synovial fluid reveal several points of interest. The content of nucleated cells varies significantly from joint to joint in the same animal and from species to species. It decreases with age within the species. In cattle, fluids with a high nucleated-cell content were obtained from joints with highly viscous synovia and a marked freedom from diseases and degenerative changes. Thus the nucleated-cell content in the highly viscous fluids in the atlanto-occipital and atlanto-axial joints was of the order of 1,200 per c.mm., while that in the much less viscous ankle-joint fluid was about 200 per c.mm. Functional differences, though obviously influencing the nucleated-cell content markedly, are not adequate to explain all the differences (Davies, 1945a). Marked degenerative changes in a human joint are often associated with raised contents of nucleated cells but not invariably so. Increased wear and tear within the human knee-joint, such as that resulting from torn semilunar cartilages, is associated with a rise in cell content generally, ranging from 300 to 700 per c.mm., rarely exceeding 1,000 per c.mm.

Red cells do not normally occur in synovial fluid though, as already indicated, even simple puncture is followed by some extravasation. Of nucleated cells, monocytes and clasmatocytes preponderate in normal synovial fluid. Lymphocytes are present in small numbers, while only very occasional polymorphonuclear leucocytes are seen. Certain cells designated as synovial cells also occur in small numbers.

Theories of Origin of Synovial Fluid

The work of Bauer and his colleagues (1940) on the composition of synovial fluid indicates that it is probably an ultrafiltrate, or dialysate, of blood plasma with the addition of mucin. The mucin cannot be a product of the articular cartilage as the two mucins are different. It is not a product of the metachromatically staining cells of the synovial membrane as these are mast cells and sulphate-free mucins do not stain metachromatically. It may arise as a secretion of the synovial cells, a view which is strongly supported by Vaubel's observations (1933a and b) that these cells in tissue culture do secrete a mucin-like substance. The identity of the latter is still awaited. Finally, the mucin may be the matrix of the surrounding connective tissue washed into the joint cavity. In this case the mucin in the joint should be of the sulphate-free and sulphate-containing types, both of which exist in the connective tissue, and should occur in the same proportion as in the connective tissue. There is no evidence that this is the case. Mucin production is probably a slow process. Aspiration of a normal joint in cattle is rapidly followed by restoration of the volume of the fluid but with considerably diminished mucin content and viscosity (Davies, 1946b).

Lubrication of the joint is obviously one of the functions of the synovial fluid. The mucin has high osmotic properties and maintains the fluid in the joint. Further, the mucin may act as a buffer maintaining the alkalinity of the fluid, in association with the calcium. Nutrition of the articular cartilage, particularly in its central portions, is almost exclusively done by the synovial fluid. All other functions must take second place to this.

I wish to thank Professor H. A. Harris for permission to reproduce Fig. 1.

References

Adkins, E. W. O., and Davies, D. V. (1940). *Quart. J. exp. Physiol.*, **30**, 147.

Bauer, W., Ropes, M. W., and Waine, H. (1940). *Phys. Rev.*, **20**, 272.

Bennett, G. A., and Bauer, W. (1932). *Amer. J. Path.*, **8**, 499.

Bruce, J., and Walmsley, R. (1937). *Brit. J. Surg.*, **25**, 17.

Bywaters, E. G. L. (1937). *J. Path. Bact.*, **44**, 247.

Coggeshall, H. C., Warren, C. F., and Bauer, W. (1940). *Anat. Rec.*, **77**, 129.

Davies, D. V. (1943). *J. Anat.*, 77, 160.

—— (1944). *Ibid.*, **78**, 68.

—— (1945). *Ibid.*, **79**, 66.

—— (1946a). *Ibid.*, **89**, 21.

—— (1946b). *Lancet*, in the Press.

Elliott, H. C. (1936). *Amer. J. Anat.*, **58**, 127.

Fisher, A. G. T. (1923). *Lancet*, **2**, 541.

Gardner, E. D. (1942). *Anat. Rec.*, **83**, 401.

Graville, A. B., and Bauer, W. (1932). *Am. Jour. Path.*, **7**, 499.

Harris, H. A. (1933). *Bone Growth in Health and Disease*. Oxford University Press. London.

Hilton, J. (1863). *Rest and Pain*. London.

Hunter, W. (1743). *Phil. Trans. Roy. Soc.*, **42**, 514.

Key, J. A. (1928). *Special Cytology*. Edited by E. V. Cowdry, Vol. II, p. 735. New York.

Lutwak-Mann, C. (1940). *Biochem. J.*, **34**, 517.

MacConaill, M. A. (1932). *J. Anat.*, **66**, 210.

Meyer, K., Smyth, E. M., and Dawson, M. H. (1939). *J. biol. Chem.*, **128**, 319.

Rosenthal, O., Bowie, M. A., and Wagoner, G. (1941). *J. Cell. Comp. Physiol.*, **17**, 221.

Todd, R. B. (1836). *Cyclopaedia of Anatomy & Physiology*, Vol. I. London.

Vaubel, E. (1933a). *J. exp. Med.*, **58**, 63.

—— (1933b). *Ibid.*, **58**, 85.

BACTERIOLOGICAL INVESTIGATION OF AIR DURING AN EPIDEMIC OF HAEMOLYTIC STREPTOCOCCAL THROAT INFECTION

PART I

BY

*C. A. GREEN, S. W. CHALLINOR

and

J. P. DUGUID

From the Royal Naval Medical School, and Bacteriology Department, Edinburgh University

Introduction

Critical reviews concerning the problems of air-borne infection have been prepared by Mackie, T. J. (1942), by Buchbinder, L. (1942) and, subsequent to the completion of the work described in this paper, by Mudd (1944) and by Mitman (1945). It is apparent that the respiratory infections are among the most important causes of ill health. In particular the relationship between nasopharyngeal infection by haemolytic streptococci and acute rheumatism has been stressed (Glover, 1930; Coburn, 1931; Collis, 1931; Green, 1942). It is uncertain to what extent respiratory tract infections are spread by air-carriage of infected droplet-nuclei or infected dust-particles. Many laboratory studies of air infection by droplet-spray, and by the raising of infected dust, have been published in recent years, but such studies do not give an account of the extent to which air-infection with pathogenic organisms occurs *naturally* in the presence of respiratory infection.

The work described below consisted essentially of an investigation of the bacterial flora of the air of the various dwelling places of a semi-closed community of youths, aged 15 to 19, during an epidemic of haemolytic streptococcal throat infections during the latter part of 1942.

Detailed observations of the bacterial content, especially of streptococci, of the air of a dormitory, the cinema hall, a recreation room, and a school-room, were made at the height of the epidemic and it was hoped that such data would indicate which parts of the daily routine of the occupants of the institution (i.e. sleeping, recreation, work, etc.) exposed them to the greatest danger of airborne infection. In addition to the bacteriological observations made under normal living conditions, observations were also made under special conditions, such as in the immediate vicinity of known sources of infection; these latter observations are described in Part II of this paper. It was hoped that the collected results of these experiments would show what degree of air-infections with the specific pathogenic organisms occurred under epidemic conditions; and what sources and mechanisms were responsible for the bulk of such infection.

Measurements of the bacterial content of the air were made with the slit sampler as designed by Bourdillon, Lidwell, and Thomas (1941) which involves suction of a measured volume of air through a narrow slit on to a revolving plate of medium placed very close (2 mm.—we used a slit—plate distance of 3 mm.) to the slit. This method yields results of considerable accuracy, and has been employed by Thomas and van den Ende (1941), Bourdillon, Lidwell, and Lovelock (1942), Challinor (1943), and by others for bacteriological observations of the air of occupied premises.

In order to facilitate identification and counting of the streptococci, a selective medium—namely, blood agar incorporating crystal violet in a concentration of 1 part in 1 million, as used by Challinor (1943), was employed. Ordinary blood-agar plates were used for observations on the total number of bacteria-carrying particles present in the air.

Epidemiological Background

The community of some 765 youths was housed in a permanent camp of single-storied buildings, designed for the specific purpose for which they were being used and placed on a low hill-top half a mile (0·8 km.) from the bank of an estuary. The institution was complete with dormitories, mess rooms, kitchens, workshops, schoolrooms, swimming baths, cinema, recreation rooms, and gymnasium. The nearest village was one mile (1·6 km.) away and some four miles (6·4 km.) off was a town of considerable size. The boys were allowed to visit both places in their leisure time but relatively few took the opportunity.

The dormitories were arranged in three separate blocks, A, B, and C, the dormitories in each block being linked together by covered corridors. These three blocks were identical in construction and

* In receipt of a grant from the Empire Rheumatism Council.

ventilation. Each dormitory measured 80 ft. × 20 ft. × 10 ft. (24 m. × 6 m. × 3 m.) and was occupied on an average by 33 boys. Apart from clothes lockers and single beds, no other furniture was present and adequate ventilation was secured by means of windows down each side of the buildings. The wooden floors were covered with polished linoleum, and the corners between floor and skirting were rounded to aid cleaning. Dormitories were swept daily; the sweepings invariably containing a considerable amount of fibre from mattresses, blankets, towels, and clothing.

The boy population joined the establishment in groups of 50 to 70 at intervals of four to six months and remained under instruction for three and a half years. On entry, a new group occupied the two dormitories at one end of block C and passed in sequence through the blocks C, B, and A during their stay at the institution. If a group became reduced in size and could not occupy all the beds in two dormitories, the vacancies were filled by members of another group.

The health of the community was very good during the summer months of 1942, but about the middle of October, tonsillitis became prevalent and was accompanied by the appearance of scarlatina, as shown in Table 1. A rise in the incidence of common colds preceded the tonsillitis wave by some weeks. Clinically, cases of scarlatina were of

TABLE 1

RISE OF EPIDEMIC BEFORE START OF INVESTIGATION

1942 period	Number of fresh cases		
	Tonsillitis	Common cold	Scarlatina
Aug. 2–Aug. 15 ..	2	2	0
,, 16– ,, 29 ..	4	2	0
,, 30–Sept. 12 ..	2	3	0
Sept. 13– ,, 26 ..	6	10	0
,, 27–Oct. 10 ..	3	11	0
Oct. 11– ,, 24 ..	13	16	4
,, 25–Nov. 7 ..	19	14	12
Nov. 8– ,, 21 ..	26	21	13

mild character without serious complications apart from otitis, which appeared in a number during hospitalization. The investigations detailed below were made during the period 13 to 29 Nov. 1942, when the epidemic was in full swing. Only one case of subacute rheumatism was recorded in the community during the following two months. The patient (aged 15½) was a member of group 3 and had been hospitalized with scarlet fever during the epidemic. Neither before nor at the time of the institutional outbreak was there any indication of an epidemic wave in the adjacent village and town, although a small number of outside contact cases appeared in households visited by the youths.

In such a community there was considerable contact in workshops, schoolroom, and recreation room between members of the three dormitory blocks, although less than that between members of different dormitories in the same blocks. Table 2 shows clearly how the epidemic was confined largely to block C, which was occupied by juniors both in actual and in service age.

TABLE 2

DORMITORY DISTRIBUTION OF EPIDEMIC CASES

Dormitory block	Group	Average age	Number in group	Estab. age in mths.*	Number of cases during period Aug. 2–Nov. 21		
					Tonsillitis cold	Common cold	Scarlet fever
C	1	15½	46	3	9	5	1
	2	15½	47	3	15	14	7
	3	15½	65	4	20	13	8
	4	16	61	8	7	7	6
	5	16	57	8	7	8	4
		Total	276		58	47	26
B	6	16	60	8	3	6	2
	7	16	58	9	3	6	0
	8	over 20	76	3	2	4	0
		Total	194		8	16	2
A	9	16½	73	14	4	4	0
	10	17½	73	26	1	5	0
	11	17	46	21	0	5	0
	12	18½	48	33	22	0	1
	13	19	55	36	2	2	0
		Total	295		9	16	1

* Time since members first joined training establishment.

Experimental Method

Each of the experiments carried out under normal living conditions may be roughly divided into three parts: (1) the period before occupation, when the air-infection was minimal; (2) the period of occupation, during which there were varying degrees of activity and varying degrees of air-infection; and (3) the period after occupation, during which air infection began to diminish. In each of these periods air samples were taken at intervals. For the majority of the observations the medium used was blood agar, incorporating crystal violet in a concentration of 1 in 1,000,000. Some observations were made using ordinary blood-agar plates in order to ascertain the numbers in the air of all the bacteria (i.e. "all organisms") which could be cultivated on this more generally favourable medium. The plates were incubated aerobically at 37° C. for about twenty-four hours and the colonies were then counted with the aid of a plate microscope. On the plates relating to each air sample counts were made of: (1) all colonies present (2) the β-haemolytic colonies resembling streptococci, and (3) the α-haemolytic colonies resembling streptococci. The results were expressed as *the number of bacteria-carrying particles per cubic foot of air*—this corresponds to the number which would be inhaled during three to six minutes.

A proportion of the β-haemolytic bacteria was filmed, tested for soluble haemolysin production, grouped by Lancefield's method, and typed by slide agglutination. Almost all the organisms examined in this way were found to be β-haemolytic streptococci of Group A and are referred to as *Streptococcus pyogenes*. Typing by slide agglutination suggested that the majority of the β-haemolytic

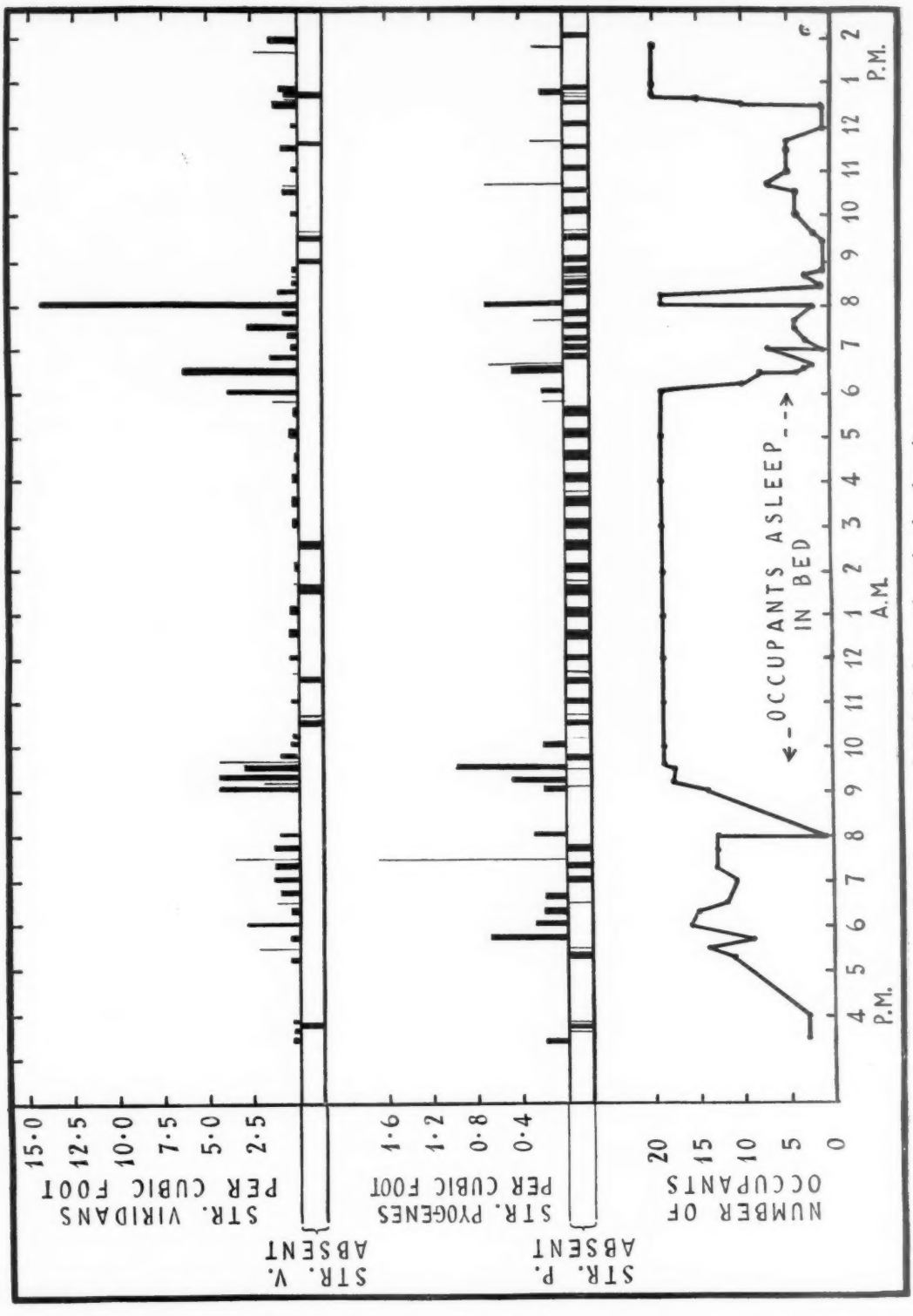

FIG. 1.—Bacteriological observations in the dormitory.

streptococci were Type 1, but the results were not entirely satisfactory and this aspect of the investigation is being continued. All strains recovered from various clinical manifestations, such as simple tonsillitis, scarlet fever, and otitis media, were of low mouse virulence, the average lethal dose being 900,000 organisms.

A proportion of the α-haemolytic colonies resembling streptococci were examined for production of green pigment on heated blood agar, morphology (chain formation) in broth culture, and for bile solubility and inulin fermentation; practically all appeared to be *Streptococcus viridans* (on the basis of these differential tests) and all were counted as such. On ordinary blood agar there were a relatively large number of staphylococcal colonies, which produced zones of haemolysis of varying types; these were distinguished from the streptococci by their larger size and opacity. Very few staphylococci grew on the crystal-violet blood-agar plates.

Bacteriological Observations in a Dormitory

The dormitory chosen was one of the two used by group 2 (Table 2) in the section which suffered most heavily during the epidemic. Of the 24 persons using the dormitory 6 were in hospital; of the remaining 18, one-third were carriers of β-haemolytic streptococci. The room was fairly large and appeared to be well ventilated. During darkness (5.15 p.m. to 7.45 a.m.) some of the windows were open behind the black-out curtains and, in fact, the presence of a small draught was noticeable in parts of the room near the windows.

The slit sampler was placed in the centre of the dormitory and was about 8 ft. (2·4 m.) from the foot of the nearest beds. Bacteriological observations of the air (75 in all) were made at intervals during 24 hours of normal occupation and the results are given in Table 3, and Fig. 1.

TABLE 3

OBSERVATIONS IN THE DORMITORY

(1)	(2)	Time	No. of occupants	Circumstances	Bacteria-carrying particles per cubic foot of air		
					All organisms	Alpha strep.	Beta strep.
				(1) *Afternoon period* 3.30 *to* 5.0 *with little occupation.*			
C	6	3.30	3	Door and windows open.		0·3	0·2
O	4	3.40	3	,, ,, ,,	8	0·3	0·0
C	6	3.45	3	,, ,, ,,		0·0	0·0
O	3	3.55	3	,, ,, ,,	6	0·4	0·0
				(2) *Evening period* 5.0 *to* 9.30 *with varying occupation.*			
C	6	5.20	11	Movement, talking, door mainly shut.		0·3	0·0
O	3	5.30	14	Blackout curtains drawn.	27	2·2	0·0
C	6	5.40	9	Changing, talking, coughing.		0·5	0·7
C	6	6.00	16	Some move, most lounge.		2·7	0·3
C	6	6.20	15	Most rest or read.		0·7	0·2
O	3	6.30	12	,, ,, ,,	48	1·6	0·0
C	6	6.40	12	Quieter.		1·2	0·2
C	6	7.00	11	More movement and talk.		1·5	0·0
C	6	7.20	13	,, ,, ,,		1·5	0·0
O	3	7.30	13	3 dance, rest, sit and talk.	51	3·5	1·7
C	6	7.40	13	3 ,, ,, ,,		1·3	0·0
C	6	8.00	13→1	Dormitory empties. Disinfection.*		1·0	0·3
C	6	9.00	14	7 in bed. Rest undressing.		4·2	0·2
O	3	9.06	16	Most in bed. Much talk.	93	1·7	0·0
C	6	9.10	18	Bedding shaken near sampler.		4·2	0·5
C	6	9.20	18	Only 4 not in bed.		3·0	1·0
O	3	9.30	18	Only 2 not in bed.	143	4·3	0·0
				(3) *Night period* 9.30 *to* 6.0, *all occupants present and in bed.*			
C	6	9.40	19	Officer inspects. Silence.		1·0	0·0
C	6	10.00	19	*All in bed.* Quiet. Sleep.		0·3	0·2
O	3	10.10	19	Quiet.	22	0·3	0·0
C	6	10.30	19	,,		0·0	0·0
O	3	10.40	19	Attendant brings in blankets for operator at 10.50.	11	0·0	0·0
C	6	11.00	19			0·2	0·0
C	6	11.30	19	Quiet.		0·0	0·0
O	3	11.40	19	,,	6	0·3	0·0
C	6	12.00	19	,,		0·5	0·0
C	12	12.30	19	,,		0·4	0·0
C	12	1.00	19	Officer visits dormitory for 1 minute.		0·3	0·0
C	12	1.30	19	Quiet.		0·0	0·0
O	3	1.45	19	,,	5	0·2	0·0
C	12	2.00	19	,,		0·1	0·0
C	12	2.30	19	,,		0·0	0·0
C	12	3.00	19	,,		0·3	0·0
C	12	3.30	19	Second operator replaces first.		0·3	0·0
O	3	3.45	19	Quiet.	7	0·3	0·0
C	12	4.00	19	,,		0·3	0·0
C	12	4.30	19	,,		0·2	0·0
C	12	5.00	19	,,		0·6	0·0
C	12	5.30	19	,,		0·1	0·0
O	3	5.45	19	,,	16	1·2	0·2

FIG. 1.—Bacteriological observations in the dormitory.

TABLE 3—*continued*

(1)	(2)	Time	No. of occupants	Circumstances	Bacteria-carrying particles per cubic foot of air		
					All organisms	Alpha strep.	Beta strep.
				(4) *Morning period.* 6.0 to 8.30, *occupants rising, dressing and leaving.*			
C	6	6.00	19	All up. Door open. Movement.		3·8	0·2
C	6	6.15	10	Coughing and bed-making.		Plate	spoilt
C	6	6.30	8→4	Shoebrushing and singing.		6·2	0·5
O	3	6.40	3	Coughing near sampler.	187	4·0	0·7
C	6	6.45	2	Quieter, changing of pillow-slips.		1·5	0·0
C	6	7.00	7→1	All away out of dormitory.		0·3	0·0
C	6	7.15	3	Bedmaking, door closed.		0·5	0·0
C	6	7.30	4	Bedmaking.		2·7	0·0
O	3	7.40	4	,,	104	1·5	0·3
C	6	7.45	4	Sweeper enters and sweeps slowly until 8.15.		0·8	0·0
C	6	8.00	2→19	Sweeping. Movement of entry. Coughing.		14·2	0·7
C	6	8.15	19	Curtains drawn open. Door open.		1·0	0·0
				(5) *Morning period.* 8.30 *to* 10.30, *with only a few occupants present.*			
C	6	8.30	1	Observer alone.		0·3	0·0
O	3	8.40	3	2 enter, cough, and leave.	5	0·3	0·0
C	6	8.45	1	Door open.		0·5	0·0
C	6	9.00	1	,,		0·0	0·0
C	6	9.30	1	,,		0·0	0·0
O	3	9.40	2	,,	5	0·0	0·0
C	6	10.00	4	Dressing and movement.		0·3	0·0
C	6	10.30	4	,, ,, ,,		0·7	0·0
				(6) *Mid-day period.* 10.30 *to* 2.0, *increasing to full occupation.*			
O	3	10.40	7	Clothes-brushing. Movement.	44	0·7	0·7
C	6	11.00	5	Ditto, and more coughing.		0·3	0·0
C	6	11.30	5	Card-playing.		0·7	0·0
O	3	11.40	5	,,	5	0·0	0·3
C	6	12.00	1	Operator alone.		0·2	0·0
C	6	12.30	1→10	Movement.		1·2	0·0
O	3	12.36	15	Standing, talking, coughing.	21	0·8	0·0
C	6	12.40	20	Movement and talking.		0·0	0·2
O	3	12.46	20	,, ,, ,,	19	0·7	0·0
C	6	12.50	20	,, ,, ,,		1·0	0·0
O	3	1.45	20	Lounging and talking.	77	2·2	0·3
C	6	2.00	20	,, ,, ,,		1·5	0·0

* Disinfection = orderly gave about 30 puffs of Dettol into the air from a "flit" gun.
(1) C = crystal-violet blood-agar plate. O = ordinary blood-agar plate.
(2) = Number of cubic feet of air sampled.

It will be seen that this experiment was divided into six periods:

(1) From 3.30 to 5.0 p.m., the dormitory was unoccupied except for the operators. The amount of air-infection was small; the average numbers of bacteria-carrying particles per cubic foot of air being: *Str. pyogenes* 0·05, *Str. viridans* 0·25, and "all organisms" 7.

(2) From 5.0 to 9.30 p.m. there was irregular occupation with variable activity, the youths coming in, going out, walking about, lounging, chatting, reading, etc. There were about twelve youths present at any one time. The amount of air-infection was considerably greater, on an average per cubic foot of air: *Str. pyogenes* 0·3, *Str. viridans* 2·1, and "all organisms" 72.

(3) From 9.30 p.m. to 6.0 a.m. the 18 occupants were asleep in bed; the operator was seated quietly at about 6 feet (1·8 m.) from the sampler. The amount of air-infection was again small being on an average per cubic foot of air: *Str. pyogenes* 0·02, *Str. viridans* 0·30, and "all organisms" 11.

(4) From 6·0 to 8·30 a.m. there was considerable activity, the youths leaving their beds, dressing, leaving and re-entering the dormitory, bedmaking and brushing their clothes; the floor was gently swept during this period. The amount of air-infection was again considerably increased, being on an average per cubic foot of air: *Str. pyogenes* 0·22, *Str. viridans* 3·3, and "all organisms" 145.

(5) From 8.30 to 10.0 a.m. the dormitory was unoccupied. The amount of air-infection was small, being on an average per cubic foot of air: *Str. pyogenes* 0·00, *Str. viridans* 0·25, and "all organisms" 5.

(6) From 10.0 a.m. to 2.0 p.m. the dormitory was occupied irregularly with variable activity. The amount of air-infection was again increased, being on an average per cubic foot of air: *Str. pyogenes* 0·15, *Str. viridans* 0·78, and "all organisms" 33.

The following points are of major interest. (1) The amount of air-infection was very small, indeed *Str. pyogenes* was almost absent, not only when the dormitory was unoccupied but also *when all the occupants were present but asleep*. (2) The bacterial content of the air diminished rapidly after the cessation of occupation or activity, for example, *Str. viridans* was present in relatively large numbers immediately before retirement (9.30 p.m.), but within twenty minutes after retirement most had disappeared. A similar rapid clearance of the considerable air-infection at 6.40 and 8.0 a.m. in the morning, was also observed. (3) The actual numbers of organisms found in the air at different times is of interest, especially the numbers of *Str. pyogenes*, which formed only a small proportion, less than 0·5%, of all the organisms which could be cultivated on ordinary blood agar. (4) The number of bacteria-carrying particles present in the air appeared to vary directly with the number of occupants and the amount of their activity. This correlation was most complete in the case of *Str. viridans*, but it appeared that the total number of airborne bacteria and the number of *Str. pyogenes* varied in the same way.

Bacteriological Observations in the Cinema

The entertainment hall, in which the cinema performances were given, was a large lofty room 90 ft. × 50 ft. × 15 ft. (27 m. × 15 m. × 4·5 m.). All the windows were shut and draped with black-out curtains, and, although the two doors were opened intermittently, the air became somewhat oppressive with the temperature rising 6° F. in about an hour. About 300 youths were present. They sat on benches arranged on either side of a central passage about 12 ft. (3·6 m.) wide, which was kept clear.

The air sampler was placed in the central passage, and was partially screened to prevent droplets from the nearest members of the audience falling directly into, or close to, the sampler. Observations (40 in number) were made and these are illustrated in Fig. 2; owing to the present restriction on paper, the tables showing detailed results are not included for this and subsequent experiments.

This experiment may conveniently be divided into three periods:

(1) From 6.30 to 8.0 p.m. the hall was unoccupied except for from two to six persons. The numbers of bacteria-carrying particles per cubic foot of air were small, averaging: *Str. pyogenes* 0·02, *Str. viridans* 0·27, "all organisms" 10.

(2) From 8.0 to 11.0 p.m. the hall was occupied. Half an hour elapsed before all 300 occupants were present. During this time there was a progressive increase in the amount of air-infection, a peak value (*Str. pyogenes* 0·7, *Str. viridans* 5·8 per cubic foot) being reached by 8.30 p.m. During occupation the bacterial

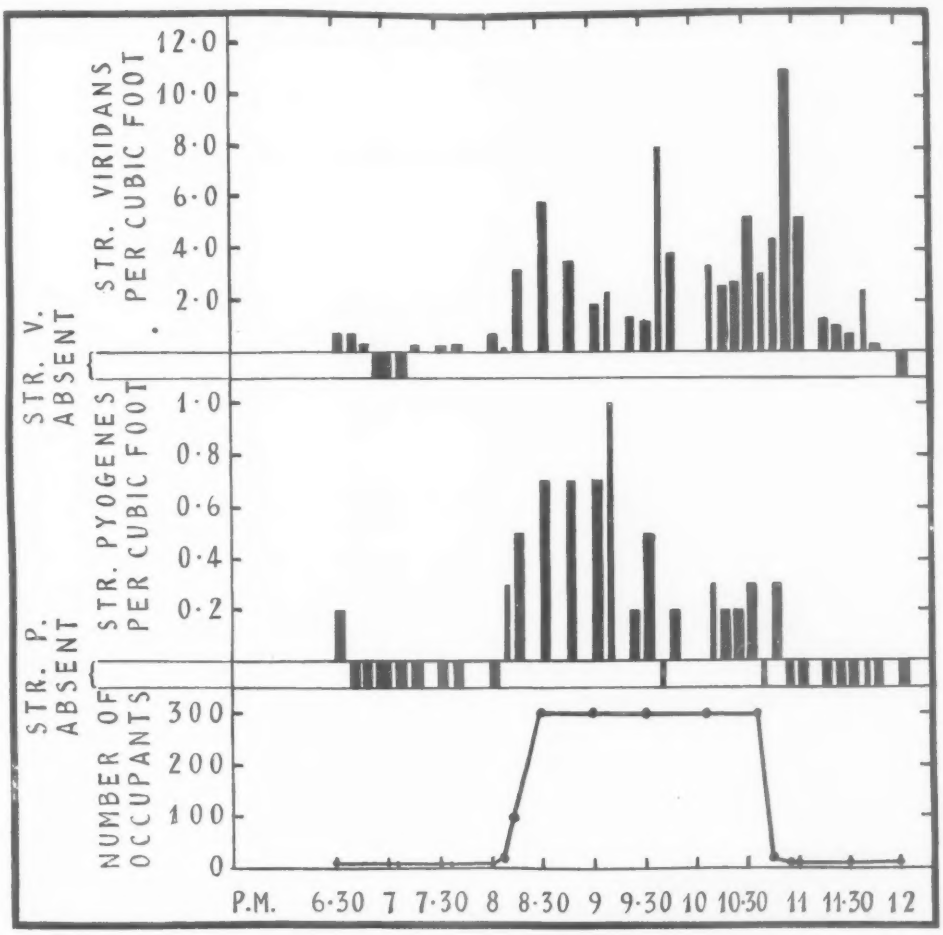

FIG. 2.—Bacteriological observations in the cinema.

content of the air varied irregularly; for the period the average numbers of bacteria-carrying particles per cubic foot of air were: *Str. pyogenes* 0·33, *Str. viridans* 3·5, "all organisms" 62. At 10.45 p.m. the occupants started to leave the hall, benches were moved, and the floor was swept; this disturbance presumably caused the high peak value recorded for *Str. viridans* at 10.53 p.m. This large amount of air-infection was rapidly cleared, there being a 90% reduction within the following twenty minutes.

(3) From 11.0 to 12.0 p.m. the hall was unoccupied except for the operator; the numbers of bacteria-carrying particles per cubic foot of air were small: *Str. pyogenes* 0·0, *Str. viridans* 1·5, "all organisms" 26.

The viridans content of the air varied irregularly during occupation of the hall and no appreciable progressive increase during continued occupation was observed. The particularly high viridans counts recorded at the beginning and end of the experiment, and at one interval during the performance, corresponded with the increased activity which prevailed at these times. It appeared, therefore, that the amount of air-infection was determined by the *degree of activity* of the occupants rather than by the number of occupants.

Small and irregular numbers of *Str. pyogenes* were found, the counts being comparable with those recorded for the experiment in the dormitory. This is of interest in view of the fact that the cinema hall was relatively (5 times) more crowded than the dormitory.

Bacteriological Observations in the Schoolroom

The schoolroom was spacious, being 100 ft. × 25 ft. × 12 ft. (30 m. × 7·5 m. × 3·6 m.). There were nine windows, all of which were closed and draped, and three doors, only two of which were used. The floor was made of dull polished wood and had been mopped three hours previous to the start of the experiment. The pupils (52 in number) were seated on benches distributed throughout the room; they made up three classes, each of which was in charge of a master who walked about and talked freely. There was little talking by the pupils; coughing was negligible and only one or

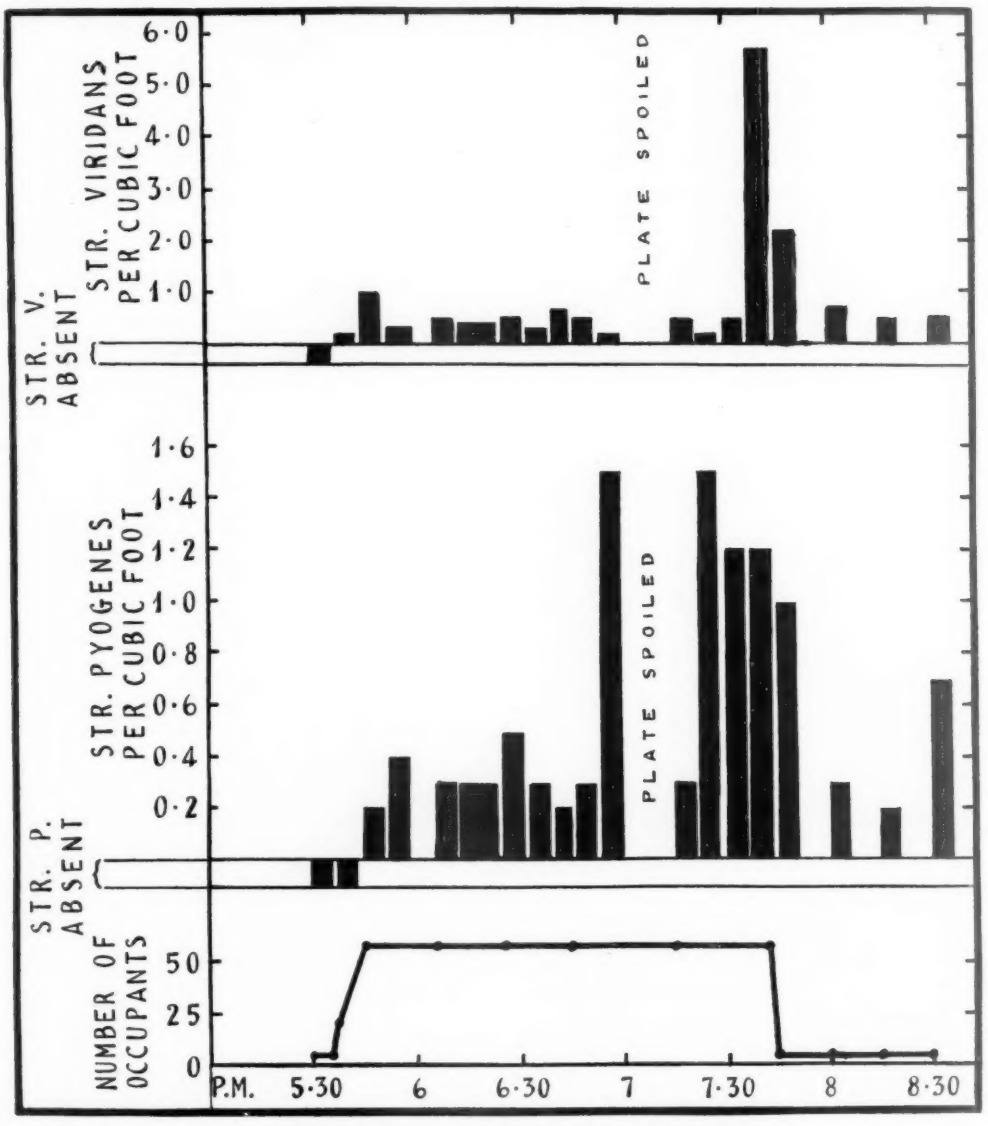

FIG. 3.—Bacteriological observations in the schoolroom.

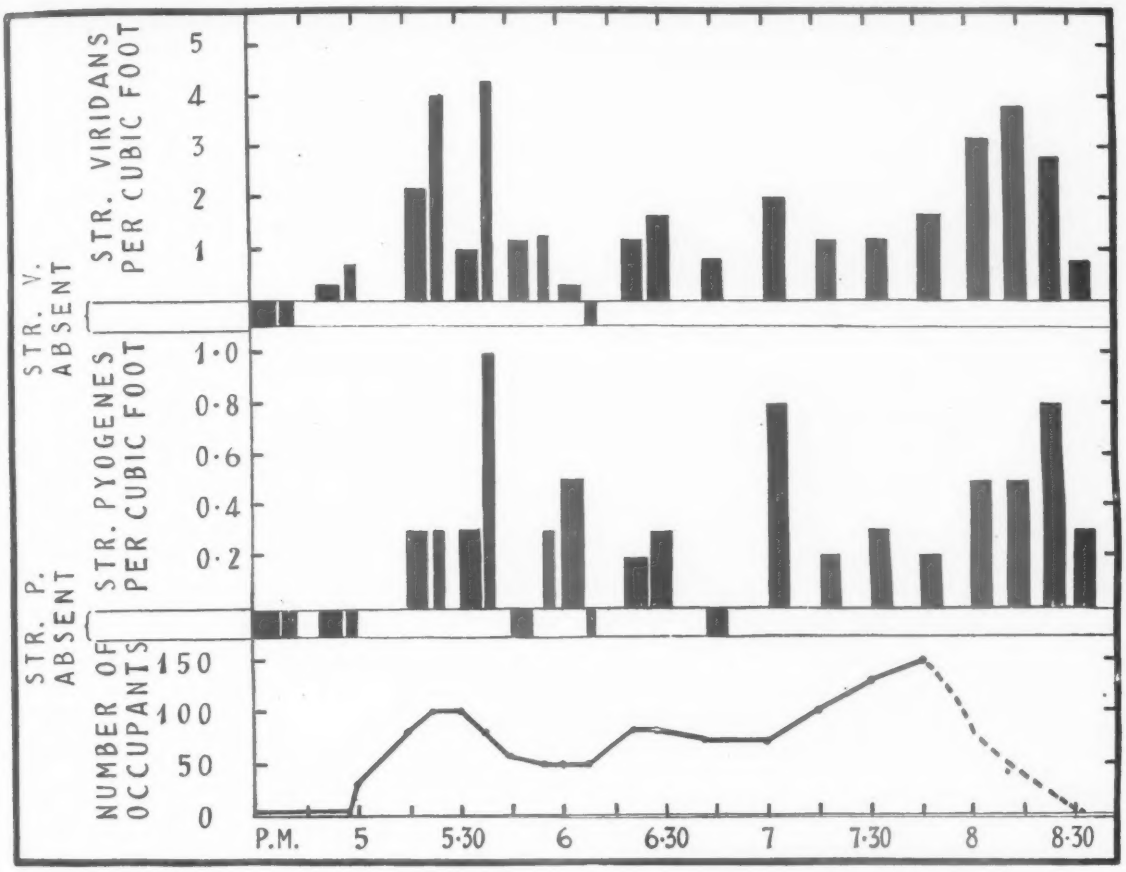

FIG. 4.—Bacteriological observations in the recreation room.

two sneezes occurred, these being far away from the slit sampler. A central position was chosen for the slit sampler, which was partially screened from the pupils in its immediate vicinity. Observations were made throughout the experiment and the results are shown in Fig. 3.

Before the room was occupied by the pupils (5.30 to 5.40 p.m.) the numbers of bacteria-carrying particles per cubic foot of air were small (*Str. pyogenes* 0·0 and *Str. viridans* 0.1. Within a few minutes of the pupils entering, the air-infection became greatly increased in amount. During occupation (5.40 to 7.40 p.m.) the average numbers of bacteria-carrying particles per cubic foot of air were: *Str. pyogenes* 0·63, *Str. viridans* 0·87, and " all organisms " 26. The large numbers of *Str. viridans* (5·7 particles per cubic foot) present in the air at the end of occupation might have been due to: (1) the increased restlessness and talking of the pupils; (2) the talking near the sampler by the master; or (3) the disturbance due to the pupils starting to leave the classroom (this occurred only during the last six minutes of occupation).

The relatively large numbers of *Str. pyogenes* also found towards the end of occupation may be similarly explained. After the end of occupation there was a rapid reduction (about 90% in twenty minutes) in the numbers of airborne *Str. viridans*. It should be noted, however, that the amount of air-infection after occupation remained for an appreciable time as great as the average amount of air-infection during occupation; during the first twenty-five minutes after occupation, the numbers of bacteria-carrying particles per cubic foot were *Str. viridans* 1·5 and *Str. pyogenes* 0·65; during the second twenty-five minutes after occupation, the numbers were *Str. viridans* 0·50 and *Str. pyogenes* 0·45.

Relatively *larger* numbers of particles carrying *Str. pyogenes*, and relatively *smaller* numbers of particles carrying *Str. viridans*, were present in the air of the schoolroom than in the air of the dormitory or cinema hall.

Bacteriological Observations in the Recreation Room

In size, the room was 90 ft. × 30 ft. × 12 ft. (27 m. × 9 m. × 3·6 m.). The floor was covered with linoleum, the windows were shut, and of the two doors one was opened intermittently. Four fan-ventilators set in the roof were moving slowly. During the two hours before the experiment the room was unoccupied. The air sampler was placed to one side of the room—about 8 ft. (2·4 m.) from the wall—and not quite half-way down the room from the door of entry at one end. The sampler was partially screened as in previous experiments. The results of the observations are shown in Fig. 4.

Before the room was occupied, the numbers of bacteria-carrying particles per cubic foot of air were small: *Str. pyogenes* 0·0, *Str. viridans* 0·25, and " all organisms " 7. During three and a half hours of occupation the number of occupants present varied between 40 and 150. They spent the time in playing cards, reading, talking, and lounging; a few of the more active occupants danced

and played games such as table tennis, etc. The atmosphere quickly became oppressive. The average numbers of bacteria-carrying particles per cubic foot of air were: *Str. pyogenes* 0·38, *Str. viridans* 1·80, and "all organisms" 65.

The bacterial content of the air was then not significantly greater than that of the air of the premises previously investigated, in which the air had seemed to be relatively fresh. The streptococcal (α and β) content of the air during the period of observation (3½ hours), varied within rather narrow limits, except for the higher counts recorded at times when there was much entering or leaving.

Discussion

In order to facilitate discussion of the observations made in the dormitory, cinema hall, school and recreation rooms, some of the more important results are summarized below, where the *average* numbers of bacteria-carrying particles per cubic foot of air, for the periods before and during occupation, are shown.*

	Dormitory	Cinema Hall	School Room	Recreation Room
Str. pyogenes (per cu. ft.)				
Before occupation ..	0·05	0·02	0·00	0·00
During occupation ..	0·22	0·33	0·63	0·38
Str. viridans (per cu. ft.)				
Before occupation ..	0·25	0·27	0·10	0·25
During occupation ..	1·91	3·50	0·87	1·80
All organisms (per cu. ft.)				
Before occupation ..	7	10	—	7
During occupation ..	74	62	26	65
Degree of crowding during occupation *				
(*a*) Average number of occupants	12	300	57	75
(*b*) Average number of occupants per 1000 cu. ft.	0·8	3·8	1·9	2·3
Degree of activity	Great	Moderate	Little	Moderate
Predominant type of activity	Ambulatory	Sedentary	Sedentary	Ambulatory

* Data for "occupation" relate only to wakeful occupation.

The magnitudes of the bacterial content of the air in the various premises, under very different conditions of occupation are of considerable interest, especially in the case of *Str. pyogenes*. Particles carrying *Str. pyogenes* were found in the air of each of the four rooms examined during the period of their occupation by the members of the establishment; the number of these infected particles per cubic foot of air varied, in different air-samples, from 0 to an upper limit of 1·7, 1·0, 1·5, and 1·0, respectively, in the four rooms; the average numbers per cubic foot of air were 0·22, 0·33, 0·63, and 0·38. From these figures, it will be seen that during occupation of such premises, a member of the establishment would be exposed, on an average, to a degree of air-infection of the order of 0·4 *Str. pyogenes*-carrying particles per cubic foot of air; this would mean that about six infected particles would be inhaled every hour. The amount of air-infection was much smaller when the rooms were unoccupied (except for the operators) and, in the case of the dormitory, when the occupants were asleep. Of all the bacteria-carrying particles recovered from the air, those carrying *Str. pyogenes* formed only a small proportion (usually less than 0·5%).

From the average findings tabulated above for *Str. pyogenes*, for *Str. viridans*, and for "all organisms," it will be seen that the amount of air-infection was much greater during occupation than before occupation. Further evidence of the dependence of air-infection upon the extent of occupation is seen in the case of the cinema hall, where the degree of crowding was greater than in any of the other rooms and the numbers of *Str. viridans* present in the air were larger. However, the degree of air-infection could not be correlated directly with the degree of crowding. For instance, the greatest air-infection with *Str. pyogenes* occurred in the school, the second least crowded of the four rooms; the greatest air-infection by "all organisms" was found in the dormitory, which was the least crowded; the *Str. viridans* concentration in the air of the dormitory was more than twice that of the air of the schoolroom, although the dormitory was only half as crowded. Furthermore, at night, when the dormitory was fully occupied, but when the occupants were in bed and asleep, the air-infection was minimal.

There appeared, on the other hand, to be a fairly close correlation between the amount of air-infection and the total amount of activity, such as walking, dressing, and other body movements. This correlation was most complete in the case of *Str. viridans* and of "all organisms"; the number of airborne particles carrying *Str. pyogenes* varied irregularly, but, as the numbers of these particles were very small, close correlation could not be expected. The amount of activity could not, of course, be measured and was assessed as far as possible by visual impression. The amount of activity which was maintained on an average over the periods of occupation was greatest in the dormitory (wakeful occupation only) and least in the schoolroom; correspondingly, the degree of air-infection with *Str. viridans* and "all organisms" was highest in the dormitory and lowest in the schoolroom. Maximal activity occurred at the beginning and at the end of the periods of occupation, when many persons were moving about (entering or leaving the room) and when there was often movement of benches and sweeping of the floor; at these times, maximum amounts of air-infection were usually recorded. Mention has already been made of the very low degree of air-infection found in the dormitory at night, when, although all occupants were present, there was practically no activity or movement.

It appears then that while the magnitude of air-infection in occupied premises depended to some extent upon the degree of crowding, it depended to a greater extent upon the amount of activity of the occupants. This suggests that a greater part of the air-infection was produced by liberation into the

air, by the activities of the occupants, of infected dust particles from clothing, floors, and furnishings, than by direct introduction of respiratory droplet-nuclei into the air. This conclusion is in accordance with the results obtained in a number of studies published in recent years. Several investigators have reported that *Str. pyogenes* are often present in large numbers on the clothing and bedclothes of infected persons, and in the dust of the floor and furnishings of the rooms occupied by these persons; moreover, some investigators have found that, in infected hospital wards, such activities as bed-making, sweeping, the toilet of the patients, and the serving of meals, regularly brought about a very great increase in the number of airborne *Str. pyogenes* (White, 1936; Brown and Allison, 1937; van den Ende, Lush and Edward, 1940; Cruickshank, 1941; Hare, 1941; Thomas and van den Ende, 1941; Wright, Cruickshank and Gunn, 1944; Hamburger, Puck, Hamburger, and Johnson, 1944; and Hamburger, Green, and Hamburger, 1945). Similar dependence of the magnitude of aerial infection upon the amount of activity likely to stir up dust has also been found in the case of counts of the total serial flora of occupied premises (Torrey and Lake, 1941; Challinor, 1943; Challinor and Duguid, 1944). Owing to the relationship between acute rheumatism and haemolytic streptococcal infection, control of the spread of the latter disease may well be expected to reduce the relapse rate in hospitals used for acute rheumatism. Coburn (1939) has utilized this procedure successfully. On the other hand, Wheeler and Jones (1942) while effecting a reduction in bacteria content of the air of one ward were not rewarded with any lowering in the incidence of throat carriers or in relapse rate. The evidence on this point is equivocal. In the present instance it must be stressed that the population at risk were normal youths, and the outbreak was not followed by a wave of acute rheumatism.

Summary

1. Observations were carried out with a slit sampler on the bacterial content of the air in various occupied premises of a residential training establishment during an epidemic of haemolytic streptococcal throat infections.

2. The average amounts of air-infection with *Str. pyogenes* in a dormitory, in a cinema hall, in a schoolroom, and in a recreation room were, respectively, 0·22, 0·33, 0·63, and 0·38 infected particles per cubic foot of air, when these premises were occupied to the extent of 0·8, 3·8, 1·9, and 2·3 occupants per 1,000 cu. ft. of room space. *Str. pyogenes* formed only a small proportion, usually less than 0·5%, of the airborne bacteria.

3. The amount of air-infection with *Str. pyogenes*, with *Str. viridans*, and with "all organisms," was appreciable only during periods when the premises were occupied; after vacation of the premises this air-infection diminished within a short time (a quarter to half an hour) to a very low level; such a low level was also found in the periods prior to occupation and, in the case of the dormitory, at night when the occupants were asleep.

(4) Air-infection depended largely upon occupation, but the amount of air-infection could not be correlated directly with the degree of crowding; closer correlation was found between the amount of air-infection and the amount of activity of the occupants. Presumably the air-infection was produced by liberation into the air of infected dust particles, this being brought about by the activity of the occupants.

We wish to acknowledge our indebtedness to Vice-Admiral Sir Sheldon F. Dudley, Medical Director General, for permission to publish this report, and to Professor T. J. Mackie for his advice and provision of laboratory facilities.

References

Bourdillon, R. B., Lidwell, O. M., and Thomas, J. C. (1941). *J. Hyg.* **41**, 197.
——, ——, and Lovelock, J. E. (1942). *Brit. med. J.* **1**, 42.
Bradley, W. H. (1932). *Quart. J. Med.*, **25**, 79.
Brown, W. A., and Allison, V. D. (1937). *J. Hyg.*, **37**, 1.
Buchbinder, L. (1942). *J. Amer. med. Ass.*, **118**, 718.
Challinor, S. W. (1943). *J. Hyg.*, **43**, 16.
——, and Duguid, J. P. (1944). *Edin. med. J.*, **51**, 280.
Coburn, A. F. (1931). *The factor of infection in the rheumatic state.* Williams and Wilkins, Baltimore.
——, and Moore, L. V. (1939). *J. clin. Invest.*, **18**, 147.
Collis, W. R. F. (1931). *Lancet*, **1**, 1341
Cruickshank, R. (1941). *Ibid.*, **1**, 493.
Glover, J. A. (1930). *Ibid.*, **1**, 499.
Green, C. A. (1942). *Ann. Rheum. Dis.*, **3**, 4.
Hamburger, M., Puck, T. T., Hamburger, V. G., and Johnson, M. A. (1944). *J. infect. Dis.*, **75**, 79.
——, Green, M. J., and Hamburger, V. G. (1945). *Ibid.*, **77**, 68.
Hare, R. (1941). *Lancet*, **1**, 85.
Mackie, T. J. (1942). *Edin. med. J.*, **49**, 607.
Mitman, M. (1945). *Brit. med. J.*, **1**, 71.
Mudd, S. (1944). *Ibid.*, **11**, 67.
Thomas, J. C., and van den Ende, M. (1941). *Ibid.*, **1**, 953.
Torrey, J. C., and Lake, M. (1941). *J. Amer. med. Ass.*, **117**, 1425.
Wheeler, D. S. M., and Jones, T. D. (1942). *Aerobiology*, Amer. Assoc. Adv. Sci. pub. No. 17, Washington, D.C., p. 237.
White, E. (1936). *Lancet*, **1**, 941.
Wright, J., Cruickshank, R., and Gunn, W. (1944). *Brit. med. J.*, **1**, 611.
Van den Ende, M., Lush, D., and Edward D. G. ff. (1940). *Lancet*, **11**, 133.

PART II

Observations recorded here were made in order to investigate more fully the mechanisms whereby infection is introduced into the air from the noses and throats of infected persons. The mechanisms considered were: (1) Direct introduction into the air of infected droplet-nuclei, during sneezing, coughing, and speaking; and (2) liberation into the air of infected dust-particles, either from the floors and furnishings of rooms, or from bedding, towels, handkerchiefs, and clothes, after these articles have been soiled by nasal secretion, sputum, or droplet-spray. Separate experiments were carried out, in each of which one of these modes of air-infection was artificially exaggerated, while the others were minimized as much as possible. Observations of the air-infection were made with the slit sampler (Bourdillon, Lidwell, and Thomas, 1941) as previously described.

Air-Infection with Respiratory Droplet-nuclei

Observations were made of the bacterial content of the air in the immediate vicinity of four " throat carriers " of β-haemolytic streptococci, who, while playing a game of cards, talked, laughed, and coughed frequently and vigorously. The game was played in the middle of the dormitory already described. This dormitory had been unoccupied for ninety minutes preceding the experiment. During the experiment, only the four " carriers " and the operator were present. The " carriers " were grouped about the air sampler, being respectively 1½, 2, 4, and 4 ft. (45, 60, 120, and 120 cm.) from it, and facing either half or fully towards it. To minimize " dust-raising " movement was restricted to the requirements of the game.

Air samples (each of 12 cu. ft.) were taken before the " carriers " entered, then at intervals throughout the game (which lasted 1 hour 40 minutes) and finally after the " carriers " had left. The findings are shown below.

Numbers of Bacteria-carrying Particles per Cubic Foot of Air

Time of Operation	Circumstances	Beta Strep.	Alpha Strep.
1.50–56 p.m.	Operator alone in dormitory ..	0·0	0·2
2.20–32 ,,	,, ,, ,, ..	0·0	0·0
2.35–47 ,,	,, ,, ,, ..	0·1	0·0
2.53–05 ,,	Four " carriers " now present,	0·0	0·6
3.07–19 ,,	playing cards quietly with an	0·0	0·0
3.21–33 ,,	occasional cough.	0·8	0·3
3.36–48 ,,	Playing noisily, with much loud	0·0	0·2
3.50–02 ,,	talking, laughter, singing and coughing.	0·1	0·3
4·04–16 ,,	Playing quietly with little talking	0·0	0·2
4.18–30 ,,	and infrequent coughing.	4·7	0·0
4.32–44 ,,	Only the operator now present in	0·1	0·4
4.45–57 ,,	dormitory.	0·3	0·0
5.00–12 ,,		0·0	0·0

During the control periods before and after the game few β streptococci were present in the air. During the game greater numbers of β streptococci were found in only 2 out of the 7 air samples taken. As both these samples were taken at times not corresponding to the period of the maximum talking and coughing, some mechanism other than the expulsion of droplet-spray may well have been responsible for this increase in the air-infection. In any case, the amount of air-infection found in the immediate vicinity of much vigorous talking, laughing, and coughing by four infected persons was very small; in fact, little greater than that found in the air at large of the institution buildings during their occupation (0·2 to 0·6 infected particles per cubic foot of air).

Air-Infection with Dust from the Floor and Bedding

Observations of the bacterial content of the air were made during sweeping and the shaking of bedclothes, in a dormitory usually occupied by 18 persons, 6 of whom were " throat carriers " of β streptococci. The dormitory had not been swept for thirty hours before the experiment.

Six youths (not carriers of β-haemolytic streptococci) were employed to raise the dust. These, as also the two operators, were masked to prevent the expulsion of droplet-spray. Dust was raised in three different ways: (1) the youths marched repeatedly up and down the dormitory; (2) they swept the floor very vigorously, especially near the sampler; and (3) they shook, close to the sampler, various blankets, towels, and pillows belonging to the usual occupants of the dormitory. Observations were made during the period of each dust raising, and also during the periods before and after. The findings are shown below as numbers of

Time of observation	Circumstances	Beta strep.	Alpha strep.	" All organisms"	Air dust
1.55–01 p.m.	Only the 2 operators present in the dormitory.	0·0	0·0		1
2.04–10 ,,		0·0	0·2		1
2.17–23 ,,		0·0	0·0		1
2.29–35 ,,	6 youths marching continually up and down the dormi-	0·2	0·8		1
2.36–42 ,,	tory.	0·0	1·0		1
2.50–56 ,,	Youths resting at far end of dormitory.	0·0	0·0		1
3.00–06 ,,	Youths sweeping floor vigorously.	4·8	*150		100
3.08–14 ,,	,, ,, ,,	5·0	*250		100
3.16–17½ ,,	,, ,, ,,			c̄2,000	
3·25–31 ,,	Youths resting at far end of dormitory.	0·0	6·6		10
3.35–36½ ,,		0·0	3·5	c̄65	10
3·40–46 ,,	Youths shaking various blankets, pillows, and towels.	7·5	*120		100
3·48–49½ ,,				c̄2,000	100
3.52–58 ,,	Several pillows beaten, one at a time, 3 ft. (0·9 m.) from sampler.	1·8	17		100
4.02–05 ,,	Only 2 operators left in dormitory.	0·7	1·0	c̄130	10

* The three highest values for alpha streptococci were estimated approximately, a part only of each plate being counted.

bacteria-carrying particles per cubic foot of air. The " dust readings " were roughly estimated from the number of dust particles observed on the surface of the culture plates with a plate microscope. They had no absolute significance, but indicate roughly the relative dust contents of the air at different times.

The results show that in the control period before " dust-raising," β streptococci were not found in the air. Only a little infected dust was liberated into the air from the floor by the youths marching up and down the dormitory. Heavy air-infection with β streptococci and other bacteria was, however, produced both as a result of vigorous sweeping of the floor and as a result of the shaking of blankets, pillows, and towels. The amount of air-infection was again greatly reduced within ten to fifteen minutes after the cessation of dust raising. The air content of visible dust particles appeared to parallel the amount of air-infection.

Air-Infection with Dust from Clothing, Towels, and Handkerchiefs

Observations were made of the bacterial content of the air of a small room—14 ft. × 14 ft. × 10 ft. (4·2 m. × 4·2 m. × 3 m.) during the shaking of their jackets, towels, and handkerchiefs, by four " throat carriers " of β streptococci. The room had, on the previous day, been emptied of furniture and hangings, and had been treated thoroughly with formalin. After the floor had been scrubbed with dettol, the room was left unoccupied until the time of the experiment. Because of these precautions, the production of air-infection by the raising of " room dust " was rendered highly improbable. To prevent the expulsion of droplet-spray, the four " carriers " and the two operators were efficiently masked while present in the room during the experiment. " Dust raising " was effected as follows: (1) the carriers marched continually round the room, thus agitating their clothing gently ; and (2) the carriers shook, in succession, their jackets, towels and handkerchiefs towards the centre of the room, where the air sampler was placed.

Air samples, each of 6 cu. ft., were taken before, during and after the " dust-raising." The findings are shown below as numbers of bacteria-carrying particles per cubic foot of air.

Time of Observation	Circumstances	Beta strep.	Air Dust
5.26 –32 p.m.	Only the 2 operators present.	0·3	1
5.33 –39 ,,		0·5	1
5·40 –46 ,,	The 4 carriers enter and march continuously round the sampler.	1·8	1
5.50 –56 ,,	The carriers shake towels, jackets, and handkerchiefs.	*150	100
6.00 –06 ,,		*200	100
6.06½–12½ ,,	Only the 2 operators present.	*250	25
6.13 –19 ,,		*150	10
6.20 –25 ,,		100	5

* These high figures for beta streptococci were derived from colony counts which were only approximate as the zones of haemolysis were, in places, confluent.

Few β streptococci were present in the air before the " carriers " entered. A small number were introduced into the air while the " carriers " marched round the room. Extremely large numbers of β streptococci were found in the air during the shaking of jackets, towels and handkerchiefs. After this " dust raising," a high degree of air-infection persisted for at least twenty minutes.

Discussion

In a critical review, Bedford (1943) has stated " there may be various opinions as to whether direct droplet-infection or airborne infection is the more important mode of transmission of respiratory disease, but there seems to be no real knowledge as to their relative importance." The demonstration by Wells (1934 and 1935), by Jennison (1942), and by Bourdillon, Lidwell, and Lovelock (1942) that large numbers of droplets, which are small enough to remain airborne as droplet-nuclei, may be expelled in sneezing, coughing, and speaking, suggested that air-infection of considerable magnitude may be produced directly by droplet-spray. On the other hand, Bloomfield and Felty (1924) and Hare (1940) found that, in the case of haemolytic streptococcal throat infections, only a small proportion of the droplets expelled in speaking, coughing, and sneezing, contained any of the pathogenic organisms. Hare, moreover, found that such haemolytic streptococci as were expelled were confined to the large droplets, and that none were present in the small droplets which remained airborne as droplet-nuclei. He suggested that air-infection was produced by the liberation into the air of infected dust particles from objects which had been soiled with the large infected droplets.

The importance of infected dust in the spread of infection has been emphasized by the findings of many investigators; *Str. pyogenes* have been found in very large numbers on the clothing and bedclothes of infected persons, and in the dust of the floor and furnishings of the rooms occupied by these persons; great increases in the number of *Str. pyogenes* in the air of wards occupied by infected persons have been found to occur during bed-making, sweeping, the toilet of patients, and the serving of meals (White, 1936; Brown and Allison, 1937; van den Ende, Lush and Edward, 1940; Thomas and van den Ende, 1941; Cruickshank, 1941; Hare, 1941; Wright, Cruickshank and Gunn, 1944; Hamburger, Puck, Hamburger, and Johnson, 1944 and 1945).

The demonstration that such air-infection is greatly reduced by dust-suppressive measures, such as the oiling of floors and bedding, has furnished further proof of the important part played by " dust-raising " in the production of air-infection (van den Ende, Lush and Edward, 1940; Andrewes, 1940; Thomas and van den Ende, 1941; Thomas, 1941). Feasby and Bynoe (1944), in circumstances similar to those recorded in the present investigation, were able to show that dust control, as apart from overcrowding, was a factor which materially influenced

the infection rate. Wright, Cruickshank and Gunn (1944) have also found dust-suppressive measures to reduce the incidence of streptococcal cross-infections in hospital wards.

The findings obtained in the present investigation accord with the view that air-infection with *Str. pyogenes* is produced mainly by the liberation into the air of infected dust from the clothing, towels, handkerchiefs, bedclothes, and environmental furnishings of infected persons, and that direct introduction into the air of infected droplet-nuclei does not occur to any great extent.

Summary

Observations were made of the amount of air-infection with *Str. pyogenes* (1) in the immediate vicinity of four " throat carriers " who, while playing a game of cards, were talking, laughing, and coughing frequently and vigorously; (2) in a dormitory which was normally occupied by " throat carriers " (but not at the time of observation), during sweeping and the shaking of bedclothes, and (3) in a room where the jackets, towels, and handkerchiefs of four " throat carriers " were vigorously shaken.

The amount of air-infection was small in the first case (on an average 0·8 *Str. pyogenes*-carrying particles per cubic foot of air), considerable in the second case (on an average about 5 *Str. pyogenes*-carrying particles per cubic foot of air), and very great in the third case (on an average, about 200 *Str. pyogenes*-carrying particles per cubic foot of air).

We wish to acknowledge our indebtedness to Vice-Admiral Sir Sheldon F. Dudley, Medical Director General, for permission to publish this report.

References

Andrewes, C. H. (1940). *Lancet*, **11**, 770.
Bedford, T. (1943). *Bull. Hyg.*, **18**, 91.
Bloomfield, A. L., and Felty, A. R. (1924). *John Hopk. Hosp. Bull.*, **34**, 115.
Bourdillon, R. B., Lidwell, O. M., and Lovelock, J. E. (1942). *Brit. med. J.*, **1**, 42.
——, ——, and Thomas, J. C. (1941). *J. Hyg.*, **41**, 197.
Brown, W. A., and Allison, V. D. (1937). *Ibid.*, **37**, 1.
Cruickshank, R. (1941). *Lancet*, **1**, 493.
Feasby, W. R., and Bynoe, E. T. (1944). *War Med.*, Chicago, **5**, 107.
Hamburger, M., Puck, T. T., Hamburger, V. G., and Johnson, M. A. (1944). *J. infect. Dis.*, **75**, 79.
Hare, R. (1940). *Canad. publ. Hlth. J.*, **31**, 539.
—— (1941). *Lancet*, **1**, 85.
Jennison, M. W. (1942). In *Aerobiology*, Amer. Assoc. Adv. Sci. pub. No. 17, Washington, D.C., p. 106.
Thomas, J. C. (1941). *Lancet*, **2**, 123.
——, and van den Ende, M. (1941). *Brit. med. J.*, **1**, 953.
Van den Ende M., Lush, D., and Edward D. G. ff. (1940). *Lancet*, **2**, 133.
Wells, W. F. (1934). *Amer. J. Hyg.*, **20**, 611.
—— (1936). *J. Ind. Hyg. Toxicol.*, **17**, 253.
White, E. (1936). *Lancet*, **1**, 941.

ANKYLOSING SPONDYLITIS:

ITS AETIOLOGY AND PATHOLOGY

BY

CHARLES W. BUCKLEY

One of the most striking features in the incidence of rheumatic diseases in the recent war has been the number of cases of spondylitis which have been met with in all branches of the Forces. At the time of the Great War of 1914–18 spondylitis was a rare disease, though the conditions to which it has often been attributed by its victims—fatigue, exhaustion, and exposure to cold and damp—were certainly no less common. The history of minor degrees of trauma within a few months prior to the onset of symptoms has been noted, and it is likely that jarring of the spine in travel in lorries over rough country, in parachute descents, or airplane crashes may be worth investigating as a contributory factor, but in a large proportion of cases no definite history of anything of the kind can be obtained. The incidence in the male sex, not less than 90%, and the tendency to attack robust and virile types rather than the weakly has been well marked. It is easy to overlook this last feature, since by the time the disease has become established the constant pain and disability may have reduced the patient's strength and vigour considerably.

Gilbert Scott advocated the name "adolescent spondylitis," as the most severe and typical cases begin within a few years after puberty; the importance of this age period will be discussed later. The cases met with in the Services usually dated the onset in the early twenties or before and it must be noted that the first symptoms may be slight and intermittent and thus overlooked. There are cases which never develop beyond a very early stage, the evidences being discovered years later under examination for other conditions. The pains in the back and limbs may be slight at first with intervals of complete freedom before the nature of the disease becomes manifest. Scott's advice that all cases of indefinite rheumatic pains appearing soon after puberty should be submitted to x-ray examination of the sacro-iliac region is sound. The diagnosis of ankylosing spondylitis may, however, be made on the basis of such an examination and prove erroneous in the light of the clinical features and the progress of the patient, therefore the x-ray examination should always be accompanied by estimation of the sedimentation rate.

Problem of Aetiology

The constitutional characters, the frequent occurrence of low-grade fever, and the sedimentation rate, raised in the great majority of cases often to a considerable degree, point to an infective origin arising from a focus, but more often than not it is impossible to identify it and removal of teeth, tonsils, and the like has rarely been found to make any impression on the disease. Oppenheimer of Beyrout (1938) has described three different types of what he terms atrophic arthritis of the spine: an acute form localized in the cervical region and due to infected tonsils; a chronic form, also chiefly affecting the upper part of the spine, of which he reports four cases—two of them had chronic amoebiasis and in one, treatment of this condition resulted in cure; and a third form which he terms ankylopoietic spondylarthritis, which is identical apparently with ankylosing spondylitis. Eleven cases of this third form are reported and in every case the patient stated that the pain in the region of the spine had followed some acute infection. Such a definite relation to infection has not been reported in Britain or America and it may be that spondylitis in the Near East differs in some respects from the forms met with in western countries; it should also be noted that amoebiasis is common in this part of the world, from 12 to 28% of the population being infected.

Boland and Present (1945) have investigated a series of 100 cases admitted to an army general hospital in the United States. They found spondylitis of the ankylosing type in 18% of patients with chronic back complaints; in 80% of the series no possible immediate cause could be found, though in 12 cases there was a history of injury to the back but not clearly related to the spondylitis. In 5 cases acute gonorrhoeal urethritis was related to the onset of back symptoms, and in 8 others an unrelated past history of gonorrhoea was elicited. In one instance a non-specific urinary infection immediately preceded the first back symptoms, which is of interest in view of the spread of the disease from a pelvic centre, which will be discussed later. Forestier (1939) suggested that the primary focus was in the genito-urinary system and recently the possibility that the prostate gland might be responsible has been mentioned (Buckley, 1943), in view of the sex incidence and the centrifugal course of the disease starting in the pelvic region. The view originally held that it was gonococcal in origin has been abandoned, since the closest investigation has failed to reveal any evidence of gonorrhoea in at

least 90% of cases, but it is well known that streptococci, staphylococci, and *Bact. coli*, among others, may invade the prostate gland, and virus infection is also a possibility. If focal infection is responsible it may act directly on the bones and joints, or by modifying the internal secretion of the prostate, or in the female by similar influence on other pelvic organs.

Robinson (1940) investigated the tuberculin-sensitivity of 45 cases of ankylosing spondylitis and found it 30% higher than that of 90 cases of other rheumatic diseases. He concluded that these results reflect either a non-specific irritant in the tuberculin used or a subclinical tuberculous state in the patient due possibly to an immunizing infection. In a previous investigation an intradermal tuberculin test was carried out and gave positive reactions in 15 out of 18 cases (Buckley, 1935). It is difficult to determine the significance of this finding in the aetiology of spondylitis.

Clinical Pathology

The clinical features and pathology are best studied in cases beginning before the union of the epiphyses in the vertebral and pelvic regions. Centres for epiphyses for the tips of the transverse processes and the spinous processes, and for the upper and lower surfaces of the vertebral bodies, appear about the sixteenth year, and those for the lateral surfaces of the sacrum about two years later, all uniting about the twenty-fifth year or later, at the same time as the epiphyses of the scapular and pelvic girdles. The epiphyses of the bones of the limbs all unite about the twentieth year, with the exception of that for the upper extremity of the tibia. In view of the association of the pathological process with actively growing bone these dates are important.

The centrifugal spread of the disease from the region of the pelvis to the vertebral column, the costo-vertebral joints, the hips, and later to the shoulders, sterno-clavicular joints, and knees but rarely beyond, is one of the most characteristic features and is invariable, though the x-ray appearances may not be uniform. In cases beginning after the union of the epiphyses, the apophyseal joints in the dorso-lumbar region and the costo-vertebral joints may show more advanced changes than those in the lower lumbar area, and the cervical spine may be extensively affected before the lumbar spine becomes ankylosed. This appears to depend on the degree of mobility; the dorso-lumbar and cervical are the regions of greatest mobility in the spinal column and movement in the costo-vertebral joints is constant, whereas the lower lumbar region may be kept at rest by muscle spasm. This point has a bearing on the question of rest or movement in treatment.

The explanation of the centrifugal progress is unknown, but recent experiments conducted by Batson (1940) to elucidate the spread of metastases from carcinoma of the prostate have thrown light upon the problem. He observed that the only anatomical system that fitted in with the distribution of the secondary deposits was the plexiform system of veins investing the prostate, the sacrum, and the iliac bones, communicating with the veins of the vertebral column. He therefore injected the dorsal vein of the penis in a cadaver with a radio-opaque pigment and observed that it spread through the venous plexus of the prostate to the common iliac, the inferior vena cava, the lateral sacral veins, and the alae of the ilium. He repeated the experiment using a thinner pigment and found that it reached the lower lumbar vertebrae and that none entered the vena cava. He then injected a monkey in the same way under anaesthesia and verified these results, but observed also that increased intra-abdominal pressure, obtained by bandaging the abdomen, prevented the dye from entering the vena cava; he concluded that straining efforts with a closed glottis would produce the same effect. With a higher pressure the injection reached the intercostal veins and as high as the base of the skull.

These veins are without valves and the flow is very slow, tending to stagnation; they appear to be storage lakes as well as pathways of drainage. Batson suggests that there are frequent reversals of flow, which might be caused by spinal movements, and proposes that in addition to the caval, portal, and pulmonary venous systems we should add a fourth—the vertebral, including the veins of the spinal column and girdles, the neck, skull and brain. Cunningham (1923) describes a thin-walled plexus of veins between the periosteum and the spinal canal. If the blood in these veins contained a morbific agent from the prostate inflammation of the dura would be likely. This may explain the features of the spondylitis described by von Bechterew in which the meninges were implicated, but since in the usual type of ankylosing spondylitis only the bones and ligamentous structures are affected there is evidently a specific affinity for these structures. Nathan (1916) observed, " whether or not these parts are involved is merely an accident of location of a generalized process and such accidental distribution provides the forms commonly associated with the names of von Bechterew, Strumpell, Marie, etc. These conditions are not essentially different, they may be chronic, transient, or progressive with or without permanent changes in the tissues involved." The importance of this observation has generally escaped notice.

Osteoporosis

In an earlier paper (1931) the opinion was expressed by the writer that the earliest recognizable change in radiographs was osteoporosis. This occurs to the most marked extent in the growing parts of the bone, as may be seen in the sacro-iliac region though the appearance may be somewhat masked by calcification of the sacro-iliac ligaments overlying the joint giving rise to an appearance of uneven density or sclerosis of the bone margins. In the bodies of the vertebrae osteoporosis is often extreme, affecting the whole of the body which thus

becomes translucent, permitting the denser lines caused by the ossified spinous ligaments or the ligaments of the facet joints to stand out conspicuously. Hilton Fagge (1877) called attention to this decalcification in his account of the first necropsy of which there is any record, and remarked that the vertebrae were so soft that they could be cut with a knife. Osteoporosis is met with in many conditions but in very few is it associated with ossification of the ligaments and tissues in its vicinity. This is sometimes seen in tuberculosis of the spine, in which Knaggs (1926) described considerable deposits of new periosteal bone and ankylosis of the vertebrae by bars of bone, which are formed by ossification of the ligaments, fibre by fibre in a uniform manner, as described by Léri (1926) in his account of ankylosing spondylitis.

In rheumatoid arthritis a similar osteoporosis occurs but without the ossification of neighbouring tissues, and in this, as in other forms of osteoporosis, the calcium removed from the bone is excreted. In spondylitis the calcium appears to be redeposited immediately in the fibrous and fibro-cartilaginous tissues in the vicinity, the ligaments begin to ossify and the joint capsules become bone, as may be seen in the facet joints of the spine and in many cases more clearly in the hip-joints. Deposition also takes place in fibro-cartilaginous tissues, such as the rim of fibro-cartilage forming the edge of the acetabulum and that of the pubic symphysis (more frequently in women than in men), but not in the articular cartilages. The outer fibres of the annulus fibrosus of the intervertebral disks become calcified, particularly those which pass from the disk to merge into the anterior and lateral ligaments, giving rise to the characteristic bridging and ultimate conversion of the outer part of the disks into solid bone. Connor (1700) described this condition very vividly. He gives an account of a skeleton which he had examined and says, " the cartilaginous edge of the vertebrae themselves were turned to perfect bone, but when I had sawed two vertebrae asunder at the commisure I found that this uniting did not enter above two lines deep." The contrast between the decalcified and softened bone of the vertebral bodies, which yield under the weight of the body [and the turgor of the nucleus pulposus of the disks] to assume the typical bobbin shape, and the marginally ossified disk, which is expanded in its centre, is very striking and characteristic. Ehrhardt records one case in which the disks were completely replaced by spongiosa continuous with that of the bodies. Deposition of calcium also takes place in the periosteum and this may be seen in the form of fringing of the bones of the pelvis.

Biochemical Factors

Resorption and redeposition of calcium in the bone is normally a continuous process. In the stage of bone growth deposition of calcium takes place at a more rapid rate than resorption, while in osteoporosis the reverse is the case, and this may be due to excessive resorption or deficient redeposition, varying in degree in different diseases. Willis (1939) in dealing with tuberculosis of bone said, " calcification of soft tissues and decalcification of bone are matters of local biochemical conditions, the former associated with anaemia and ischaemia, and the latter with active hyperaemia," but this is inadequate to explain all forms, such, for example, as senile osteoporosis. The osteoporosis of spondylitis must be considered in association with the characteristic deposition in the adjacent tissues.

The problem of calcification as an essential stage in bone growth has been the subject of research for many years, but for the most part as a normal physiological process and so far as the writer is aware the process as it occurs in ankylosing spondylitis has not received attention. Robison and Soames (1924) put forward a hypothesis based on experiment which has been the foundation of much of the subsequent work. They noted that the osteoblasts, the hypertrophic cartilage cells, and certain cells of the inner portion of the periosteum in a growing bone contain, or can secrete, a very active enzyme, which by hydrolysing the salts of phosphoric esters brought to the ossifying zone by the blood stream caused a local increase in the concentration of phosphate ions. The solubility product for calcium phosphate, which is probably nearly reached in circulating plasma at normal *p*H, is thus exceeded locally and a deposition of calcium phosphate takes place in the neighbourhood of the cells which secrete the enzyme. This enzyme is a phosphoric esterase or phosphatase and there are several varieties, those of bone, kidney, and intestinal mucosa are " alkaline " phosphatases while that secreted by the prostate and some other organs is the " acid " phosphatase; by these terms is meant that the optimum substrate *p*H is over 7 for the alkaline and under 7 for the acid form. In carcinoma of the prostate with metastases in bone the acid phosphatase is greatly increased, and this observation led to speculation as to the possibility that it might also have a bearing on the aetiology of ankylosing spondylitis. Different methods are in use for measuring the amount of phosphatase in the plasma. Race (1945) in a series of 13 cases of spondylitis found the average level of acid phosphatase was 2·2 by a method in which the normal maximum is taken as 4 units; the highest figure obtained was 3·8 and the lowest 0·9. While the number of cases is insufficient to justify any sweeping conclusion it indicates fairly clearly that " acid " phosphatase has probably no bearing on ankylosing spondylitis.

The alkaline phosphatase on the other hand showed a slight increase in plasma in a series of cases reported by the writer (1935), the average being 0·34 (Kay units) compared with a normal maximum by this method of 0·20; a few additional cases examined since have been within the same range. The presence of phosphatase in the plasma is for the most part due to its passage from the tissues, and Kay (1932) suggested that it might arise from leakage from the bones and that such leakage might be the cause of irregular deposition of bone outside the usual sites. The types of phosphatase from the bone, kidney, and intestinal mucosa are identical in their power of hydrolysing phosphoric esters *in vitro*, but experiments *in vitro* may not adequately account for what happens in the living body, and it has been suggested that the cells in bone develop their enzyme for the specific object of calcification, those of the intestinal mucosa to effect the breakdown of phosphoric esters in the food (Kay, 1932), and those of the kidney to convert phosphoric esters to the inorganic phosphates which are excreted in the urine (Eichholz, Brull, and Robison, 1925). The kidney, however, may calcify if the blood supply is interfered with (Remesow, 1925).

In rickets calcification does not take place in the bone in spite of the fact that there is a high level of phos-

phatase in the zone of hypertrophic cartilage. This appears to be due to the low inorganic phosphate content of the circulating blood (Kay, 1932). The deficient calcification in the cartilage zone in rickets may throw some light on the rarefaction of bone in spondylitis. It is essential for the calcifying process that in addition to the presence of the enzyme there should be an adequate supply of phosphoric esters for it to act upon. In the absence of this, calcification does not take place, but it is not clear whether such a deficiency could exist in the bone and not in its vicinity where calcification does occur in spondylitis. Leriche and Policard (1928) point out that precipitation of bone salts depends less on the blood than on the lymph, and such material might be abundant in lymph but much less abundant in the blood.

The *p*H *in vitro* has an important bearing on the process of hydrolysis. The activity of bone phosphatase is at its maximum with the esters which are believed to form the most probable substrate between 8·4 and 9·4, increasing with the increase in alkalinity; this may also influence the process *in vivo* since the *p*H of the blood is 7·4, at which level the activity would probably be very low. Page (1930) states that the mobilization of calcium and phosphorus from the bone is a process in which diminution of the activity of bone phosphatase is the first step. The toxic material which is responsible for the pathology of spondylitis may possibly act by lowering the *p*H of the bone cells and thus diminishing the phosphatase activity, acting as an inhibitor. Another factor may call for consideration—namely, the presence or absence of activators. It has been shown (Jenner and Kay, 1931) that magnesium has an activating effect on bone phosphatase, and they put forward the suggestion that this may be important in the therapy of some bone diseases. The value of aluminium acetate in osteitis deformans may be due to an action of this nature, furnishing a parallel.

While hydrolysis of phosphoric esters is the usual function of phosphatase, there is some evidence that reverse action may take place—synthesis of the ester from inorganic phosphate of calcium. This has been demonstrated *in vitro* and Kay (1932) says, " it may be that the enzyme plays an active part also in bone resorption and demineralization under both normal and pathological conditions by synthesizing, from some of the insoluble calcium phosphate of the bone, soluble phosphoric esters of calcium. It is not impossible, though perhaps unlikely, that the synthetic as well as the hydrolytic activity of the enzyme plays a part in normal bone formation, that the effect of the enzyme is diphasic, producing synthesis of phosphoric esters in one part of the ossifying zone and hydrolysis with deposition of calcium phosphate in another." If this suggestion should be confirmed it would throw light on the process in ankylosing spondylitis and also in rickets.

It appears reasonable in the light of these biochemical findings and the anatomical path of the disease to conclude that ankylosing spondylitis is due to the action of a toxin, which may be bacterial or may be due to the high metabolic activity of the prostate at the age at which the disease is most virulent. The greater activity of phosphatase in the region of the epiphyses before their union also accounts in part for the greater severity of ankylosing spondylitis in the young. It is obvious that after the epiphyses have joined up the effects will be modified, but it must be remembered that resorption and redeposition of calcium is a continuous process even in adult bone, though at a slower rate. Both osteoporosis and new bone formation are much less pronounced in cases beginning after the age of 25 or thereabouts and this has an important bearing on prognosis, which is then much more favourable; in fact, such cases sometimes become arrested without any specific line of treatment.

It will be useful to compare rheumatoid arthritis, rickets, and spondylitis as three diseases presenting osteoporosis, in view especially of the common confusion between arthritis and spondylitis. In arthritis, osteoporosis, may be extreme but is not directly associated with the epiphyseal area nor with the period of active growth. In arthritis the plasma phosphatase is not increased, in spondylitis a moderate increase is usual, and in rickets the increase is generally considerable. In arthritis, ankylosis only occurs as a terminal event after the breakdown of the articular surfaces; in spondylitis and in rickets there is no tendency to breakdown of the bone structure but softening may lead to deformity, owing to the effects of weight and posture ; there is new bone formation in the ligaments and joint capsules in spondylitis leading to early ankylosis, and sub-periosteally in both. In arthritis the joints are the chief seats of damage, beginning with synovial inflammation, but in spondylitis the damage in the joints is probably due to extension from the bone through the articular cartilage which does not contain phosphatase until it becomes vascularized (Goodwin and Robison, 1924), and to the spread of calcification from the ligaments and capsules.

Influence of Sex Hormones

The evidence as to the source from which the disease appears to start leads to consideration of the possible influence of the sex glands on its development. It is noteworthy that it so often attacks youths of robust and virile type soon after puberty, and there has been evidence in some of my cases of high activity of sexual functions. There is some evidence that the sex glands have an influence on bone formation. Paterson (1929) states that hyperactivity of the sex glands accelerates fusion of the epiphyses, and castration delays ossification. It is uncertain whether this is a direct action or through the medium of other glands, the thyroid or pituitary. Gardner and Pfeiffer (1938) concluded from experiments that testosterone propionate inhibits skeletal changes which occur when oestrogens are injected over a long period. Silberberg (1939) described complex changes in ossification under the influence of oestrogen administration, with ossification of intercartilaginous ground substance in the epiphyseal disks, ribs, and vertebrae. From the clinical aspect the condition formerly described as senile osteoporosis but which is now known not to be limited to ages which may be regarded as senile, and to which the name post-menopausal spondylitis has also been applied, has some bearing on the problem. It is more common in women, developing soon after the menopause in many cases, but Burrows and Graham (1945) in an exhaustive study of spinal osteoporosis appear to attach importance not to the sex glands but rather to dietetic deficiency, especially to the possible effect of vitamin C. The

same factors appear to apply to puerperal osteomalacia.

Albright and his colleagues (1940) showed that after the menopause women are prone to develop osteoporosis of the pelvis and spine, which can be corrected by oestrogen therapy; the long bones are rarely affected, which differentiates it from hyperparathyroidism. In Cushing's syndrome osteoporosis is a symptom and oestrogen formation is decreased and urinary androgens are increased. From these scanty data it is impossible to assume with certainty that the sex glands have any influence in spondylitis. Freiberg (1942) found no benefit from the administration of oestrogens in spondylitis but other observers are still studying this possible line of treatment.

Sequence of Changes in Spondylitis

It is now desirable to consider the sequence of the changes in spondylitis and their association with the pathological and biochemical changes. The first definite objective evidence in x-ray films is osteoporosis beginning in the region of the epiphyses of the sacro-iliac joints, in the bodies of the lower lumbar vertebrae, and in their articular processes. It may be due to toxic substances conveyed in the blood from the region of the prostate. Marie and Léri (1908) described spondylitis as primarily an infectious or toxic rarefying osteopathy, a definition with which the present writer agrees, holding that it is definitely not a form of rheumatoid arthritis. The osteoporosis may be due to excessive resorption of the inorganic calcium phosphate, or alternatively to failure in the normal process of redeposition. This may be due to diminished production of phosphatase, but it is to be noted that in rickets where the level of phosphatase is raised osteoporosis occurs; or to lack of adequate substrate; or to a *p*H unfavourable to its action; or possibly to a reversal of the normal action of the enzyme which has already been mentioned. Leakage of phosphatase from the bone to the adjacent subperiosteal region and the ligaments takes place, and deposition of calcium phosphate follows. This may be derived from the mobilized calcium phosphate from the bone which has there been converted into phosphoric esters and may be conveyed in the lymph channels, or to the calcium phosphate of the plasma, which is, however, small in amount. The deposit is at first calcium phosphate or a more complex salt of calcium which becomes converted into true bone, but if intermission in the disease occurs the calcium salt may be reabsorbed. This explains the fact that radiographs under such conditions often show a degree of improvement in the bony changes that might be thought impossible. Hilton Fagge in the report of the necropsy already referred to, noted that, "an opaque, white, mortar-like substance filled the cancellous spaces at the head of the ribs, the femur, and the innominate bone, and a similar material was deposited here and there about the outer surface of the arches." This was evidently the calcified material which was about to undergo transformation into bone.

There is an obstacle to the full acceptance of the theory of the spread of the disease through the prostatic plexus and vertebral veins—namely, that the knees are occasionally affected in severe cases and it is not possible to assume a backflow in the veins which would go as far as the knees. It may be that they are attacked through the toxic material entering the vena cava in small amounts. In such a case, however, it might be argued that the small joints of the limbs would be equally open to attack, which in my experience occurs so rarely in true ankylosing spondylitis as to be of importance in differential diagnosis. The latter part of this statement may be disputed but in a study of over 200 cases the writer has never seen a case in which the small joints of the hands and feet were affected in true ankylosing spondylitis. In 3 cases which showed arthritis in the hands and feet the condition was evidently a gonorrhoeal arthritis; in 2 others the feet and hands were affected long before the spine and the condition was rheumatoid arthritis spreading to the vertebral joints.

The true joints of the vertebral column, those between the articular processes, are naturally liable to be attacked by the same diseases as those of the rest of the body, and this occurs in rheumatoid and gonorrhoeal arthritis, in tuberculosis, undulant fever, dysentery, and other conditions, but a critical examination of the history and the radiographic appearances will generally serve to differentiate these forms of arthritis from ankylosing spondylitis. Centrifugal progression from a pelvic focus, marked osteoporosis and deposition of calcium around the joints, and bony ankylosis without bone destruction are cardinal features. The radiographic appearances of an ankylosed hip-joint in spondylitis, in which the head of the femur appears practically intact and the bony trabeculae extend from the pelvis to the shaft of the femur along the lines of stress, is in marked contrast to the appearances of an ankylosed joint in rheumatoid arthritis. The ossification of ligaments may be seen in other diseases in accordance with the so-called law of Wolf and Holzknecht; "every tissue which is submitted to an excessive pressure or strain reacts by such type of formation as is best adapted to withstand it." The new bone formation in spinal tuberculosis has already been referred to, but in this and other diseases the relentless centrifugal progress is lacking.

Some Characteristic Symptoms

Pain is generally the first sign of the onset of the disease and may be indefinite in distribution without objective evidence, but three general types may be recognized.

Referred pains from the region of the sacro-iliac joints will be felt in the area of distribution of the lower lumbar and upper sacral nerve roots, and from the hip-joint will be felt along the inner aspect of the thigh and knee, and these sciatic pains are among the earliest signs.

Girdle pains occur in the active phase in the lumbar and dorsal regions, but it rarely happens that the foramina are actually obstructed by calcareous deposit; the pain is due to local congestion and swelling in the region of the foramina and to the affection of the costo-vertebral joints; any movement of the affected parts of the spinal column will be painful.

In the later stages pain will be due to stiffness or ankylosis and difficulties of posture, such as may be experienced when the joints have become ankylosed in a bad position.

The facies and gait are often characteristic even in an early stage. Muscle wasting is not conspicuous until the disease is well advanced and is due to disuse, contrasting with the trophic wasting of acute rheumatoid arthritis. Iritis is noted in about 10% of cases and was first reported about twenty years ago at a meeting of the Brussels Ophthalmological Congress. This was marked in one of my cases, a woman in whom the disease appeared to be related to a form of colitis or dysentery from which she suffered recurrent attacks. This is of interest in view of the cases associated with amoebiasis already referred to; in this case there had been no search for amoebic infection so far as the writer is aware. The occurrence of iritis has been cited as evidence that spondylitis is a form of rheumatoid arthritis but can carry no weight as an argument; it is probably due to rubbing the eyes with infected fingers.

Boland and Present (1945) have discussed fully the symptoms and radiographic appearances in a study of 100 cases, and set forth the evidence for and against the view that ankylosing spondylitis is a form of rheumatoid arthritis. They accept their identity—a view commonly held in America—but the arguments as stated by them against such a conclusion appear to be very strong. Oppenheimer (1938) is also of this opinion but the problem calls for further investigation; the evidence submitted in this paper points in the opposite direction.

Although this paper is not concerned with treatment reference to a report on the use of gold may be made as it has a bearing on the nature of the disease. Sherwood (1940) in discussing gold treatment in arthritis stated that haematuria only occurred in cases of ankylosing spondylitis and he had met with it frequently in that disease. It was his experience, which is generally shared, that gold was rarely of service in spondylitis; the writer would go further and suggest that if benefit followed the use of gold in a case of spinal arthritis it was probably rheumatoid arthritis of the spine and not true ankylosing spondylitis.

Summary

The aetiology and pathology of ankylosing spondylitis are discussed in the light of Batson's work on the venous circulation from the prostatic plexus.

The influence of phosphatase on bone resorption and redeposition is described, and the possibility of a toxin from the prostate influencing this process is considered.

The bone changes in rheumatoid arthritis, spondylitis, and rickets are compared, and the conclusion is drawn that ankylosing spondylitis is not a form of arthritis but a toxic osteopathy.

The possible influence of sex hormones is discussed and found to be " not proven " but calling for further investigation. The importance of the dates of union of the epiphyses and the bearing of this on the disease is mentioned; the effect of the age at onset on the prognosis in the light of the pathology is pointed out.

Further investigation is urgently required in view of the great increase in the incidence of the disease, particularly in those cases which do not conform strictly to the classical pattern, since their inclusion in lists of cases used for drawing statistical and other conclusions is responsible for confusion.

References

Albright, F., Smith, P. H., and Richardson, A. M. (1941). *J. Amer. med. Ass.*, **116**, 2465.

Batson, O. V. (1940). *Ann. Surg.*, **112**, 138–149.

Boland, E. W., and Present, A. J. (1945). *J. Amer. med. Ass.*, **129**, 843.

Buckley, C. W. (1931). *Brit. med. J.*, **1**, 1108. (1935). *Rep. Chr. Rheum. Dis.*, **1**, 77. London. (1943). *Brit. med. J.*, **2**, 4.

Burrows, H. J., and Graham, G. (1945). *Quart. J. Med.*, **14**, 147.

Connor, *Philosoph. Trans.*, 1700. Quoted by Llewellyn Jones *Arthritis Deformans*. Bristol, 1909.

Cunningham, D. J. (1923). *Textbook of Anatomy*, p. 711.

Eichholz, F., Robison, R., and Brull, L. (1925). *Proc. roy. Soc. Lond.* (B), **99**, 91.

Fagge, C., Hilton (1877). *Trans. path. Soc.*, **28**, 201.

Forestier, J. (1939). *Radiol.*, **33**, 389.

Freiberg, J. A. (1940). *J. Amer. med. Assn.*, **115**, 2210.

Gardner, W. U., and Pfeiffer, C. (1938). *Proc. Soc. Exp. Biol. & Med.*, **38**, 599.

Goodwin, H. W., and Robison, R. (1924). *Biochem. J.*, **18**, 1161.

Jenner, H. D., and Kay, H. D. (1931). *J. Biol. Chem.*, **93**, 733.

Kay, H. D. (1932). *Phys. Rev.*, **12**, 384–422.

Knaggs, R. L. (1926). *The Inflammatory and Toxic Diseases of Bone*. Bristol.

Léri, A. (1926). *Étude sur les affections de la Colonne Vertébrale*. Paris.

Leriche, R., and Policard, A. (1928). *The Normal and Pathological Physiology of Bone*, p. 57. St. Louis.

Marie, P., and Léri, A. (1906). *Nouvelle Iconographie de la Salpetriere*, **19**, 32.

Martland, M., and Robison, R. (1924). *Biochem. J.*, **18**, 1354.

Nathan, P. W. (1916). *Amer. J. Med. Sci.*, **152**, 667.

Oppenheimer, A. (1938). *J. Bone & Joint Surg.*, **20**, 285–313.

Paterson, R. S. (1929). *Jour. Anat.*, **64**, 28.

Race, J. (1945). Personal communication.

Remesow, I. (1926). *Biochem. Zeitschr.*, **168**, 239.

Robinson, G. (1940). *Ann. Rheum. Dis.*, **2**, 41.

Robison, R., and Soames, K. M. (1924). *Biochem. J.*, **18**, 740.

Scott, S. Gilbert (1942) *Adolescent Spondylitis*. Oxford Medical Publications. London.

Sherwood, K. K. (1940). *North West. Med.*, **39**, 452.

Silberberg, M. and R. (1939). *Arch. Path.*, **28**, 340.

Willis, T. A. (1939). *Trans. Nat. Tuberc. Ass.*, **35**, 73.

ORTHOPAEDIC ASPECTS OF RHEUMATOID ARTHRITIS

BY

JOHN BASTOW

Attainment of an improved bodily posture is of the utmost importance if the general resistance of the individual to the infection is to be upgraded. The typical posture of rheumatoid arthritis is one of fatigue, with " poking chin," drooping shoulders, flat chest with poor respiratory excursion, visceroptosis, sway-back from the waist, flexed knees, and pronated feet. The key-note of the corrective process is rest and remedial exercises—done at first in recumbency to eliminate the effects of gravity. Abdominal breathing, and pelvic tilting with gluteal and quadriceps contractions, can be practised by the most toxic patient, and as the general condition improves postural training in correct sitting, standing, and walking attitudes should be given. A firm mattress is a *sine qua non*. The interior-spring mattress and the feather bed should be firmly condemned.

With local articular lesions in the acute stage the most important single aim is the prevention of deformity and the provision of rest by local splintage. The only satisfactory splintage is " tailor-made " on the patient, and this, in most cases, is provided by light plaster of Paris casts. Castex splints and easily moulded light aluminium splints are successfully used, and there is an increasing use of plastics, such as perspex, but at present these need to be made on a plaster cast. Particularly insidious early deformities to be watched for are: (*a*) ulnar deviation of the fingers at the metacarpo-phalageal joints; (*b*) flexion contracture of the wrists; (*c*) adduction contractures of the shoulders; (*d*) backward and outward subluxation of the knees; and (*e*) pronation of the feet.

Hands.—Hands are best dealt with by: (1) Rest plasters worn at night to afford complete support to the fingers and wrists; and (2) short cock-up plasters by day, which allow free use of the fingers and thumb and so do not make the patients helpless.

Shoulders.—Shoulders are difficult to splint satisfactorily, and in the acute phase there is no substitute for the abduction splint, usually of well-padded Cramer wire or duralumin.

Knees.—Knees are particularly suitable for plaster correction, and the plasters should always be complete—extending from toes to groin. In the knee early flexion contracture has an especially vicious effect by increasing the weight-bearing strain on the articular cartilage, owing to the increased leverage when the patient is standing up.

There are three stages of flexion spasm of a joint which is the site of *acute* arthritis: (1) where there is flexion spasm which is abolished by rest; (2) where there is flexion spasm abolished by anaesthesia; and (3) flexion deformity, where secondary contracture of muscles and ligaments has occurred and correction cannot be obtained by rest and anaesthesia alone.

In the *subacute stage* there are: (1) some degree of deformity that requires correction; and (2) danger of relapse or insidious onset of further deformity if corrective splintage is not instituted.

In the *chronic stage*, with established deformity, the corrective measures necessary often include operation, such as arthroplasty or arthrodesis.

Principles of Splintage

A. Rest combined with daily exercises to prevent development of adhesions, which are prone to occur early in this disease; ideally, 23½ hours splintage, with half an hour's exercise during day.

B. Rest must take place in the optimum position for function.

C. If deformity exists it must be corrected so far as is compatible with the degree of tissue damage, either by: (*a*) anaesthesia only, followed by plasters; (*b*) serial plasters; or (*c*) manipulation under anaesthesia, and plasters.

Fallacies.—" Too acute for splintage." No case is too acute for splintage. The more active the joint inflammation the greater need for the rest and relief from spasm that splintage ensures.

" Do not manipulate for fear of flaring up inflammation." There is no need to fear any flare-up of inflammation provided manipulation is followed by splintage and too much correction is not attempted at one sitting.

" Joints will get stiff if rested or splinted; keep going at all costs." This is not true. Joints, if splinted, will not stiffen provided they are allowed one period of movement daily with non-weight-bearing exercise. The quickest way to destroy, and consequently stiffen, a joint is to exercise it excessively when it is hot and swollen.

" Manipulation will increase the range of movement." This is not necessarily so in rheumatoid arthritis. If a patient has knees flexed habitually to 90 degrees with a further range of active flexion to 60 degrees (i.e. 30 degrees range in all), then if you straighten these knees by serial manipulations and plasters until they are extended to 180 degrees, you will find the active range of flexion still 30 degrees, i.e. 180 degrees to 150 degrees. For this reason you must be careful in selecting your cases for manipulation, and not transform a comfortably seated cripple to an uncomfortable standing one who cannot sit.

Points of Technique

Plasters applied under anaesthesia without manipulation can be unpadded, smoothly applied

with slab technique and encircling bandages laid on and never pulled tight. The patient should be given one dose of morphine after the anaesthetic, and then pot. brom. gr. 20 (1·3 g.), aspirin gr. 10 (0·65 g.), four-hourly for forty-eight hours, when the plasters are split and the joints given daily physiotherapy.

Serial plasters are applied under the influence of a sedative, without manipulation, and split when dry. The patient wears the plasters continuously except for daily physiotherapy; gain in movement is measured weekly. When progress comes to a standstill, then new serial plasters are applied in the best position obtainable and the routine is repeated. Plasters are usually changed at three-weekly intervals.

In manipulation and plaster under anaesthesia controlled force is used, adhesions are broken down and contracted muscles stretched. One must never do too much at one session.

In the case of the knee a gain of anything from 10 to 30 degrees in extension is aimed at, and then plasters are applied with the pressure points padded with felt and gentle corrective pressure maintained until the plaster sets. These plasters are split in forty-eight hours and the patient is given sedatives regularly. The subsequent routine is the same as for serial plasters without anaesthesia.

When activity ceases and the patient is allowed up some splintage is often necessary, at first to counteract the effects of gravity. Light guarding plasters for the knee, wedged heels and arch supports for the feet, ankle steels and T-straps for the ankle, knee-cages and calipers, etc., all have their uses. Gradually an osteoarthritic phase supervenes, when the joint is creaky but no longer painful, and apparatus can often be discarded but must be re-applied at the first signs of re-activity. Night splints are of great use in this stage, and their use should be continued as long as possible. Finally, rehabilitation should take into account the individual's future mode of life, and he or she should, so far as possible, plan their existence to avoid too heavy a strain on their physically handicapped limbs. The Government's Register of Disabled Persons should be of great assistance in securing for these people priority of suitable light jobs and sheltered occupations.

RETURN TO NORMAL OF X-RAY CHANGES IN RHEUMATOID ARTHRITIS *

CASE REPORT

BY

MARCELLO LUCCHESI and OSWALDO LUCCHESI

Our principal object is to present this case from the radiological aspect because of the progressive retrogression and total disappearance of the organic articular lesions. This observation we believe to be unique. We have not come across any mention of the return to normal of the radiological features, either alone or concomitantly with the clinical cure of arthritis. We know that pathological articular lesions once produced have a tendency to progress in spite of treatment or suspension of clinical evolution. The improvement in radiological changes, once obtained, is not proportional to the clinical improvement, being very much slower and showing an extinction of activity of the destructive lesions rather than a reparative process. However, with the improvement in the general condition of the patient, or his articular functions, radiological lesions develop much more slowly or even become stationary, as a consequence of the clinical inertia of the disease.

Morrison and Kuhns (1936) were the first to take up the study of the evolution of the alterations observed by x rays in 73 cases of chronic arthritis, 55 of which were rheumatoid arthritis. There was a history of some months duration in 6 cases, there were 5 cases of one year's duration, and 21 cases of over five years. Among these patients, the radiological observations covered a period of from four to ten years from the first to the last observation. In 49 cases, the radiological findings became worse; 4 cases showed no appreciable alteration; and in only 2 cases were there improvements in the radiological findings—a decrease of the bony deformity and disappearance of the destructive articular changes. Clinically, 22 cases deteriorated, 7 were stationary, and 26 improved. From these statistics one may come to the conclusion that there is no parallelism in the evolution of the radiological and clinical pictures. There was a high proportion of cases showing clinical improvement together with radiological deterioration. Morrison and Kuhns concluded that real improvement in the radiological findings is rarely seen. The case report which follows should be considered in the light of their findings.

Case report

History.—J. C., a white girl aged 21 years, complained of articular pains for about seven months; before this she had nothing abnormal. Then she began to note a slight loss of weight, anorexia, nervousness, indisposition for her work, fatigue, weakness, and nervous irritability, which provoked frequent outbursts of crying. Together with these prodromal symptoms she observed an increase in the size of the proximal interphalangeal joints of the middle fingers, without however feeling any pain. Four months later she began to feel continuous throbbing pains in the knees, which did not increase in size but showed cutaneous hyperthermia; the pains became very intense, making it impossible for the patient to walk. At the same time the process attacked the right wrist, causing swelling, warmth, acute pain, and marked functional disability. Some days afterwards the left wrist was also involved and in less than a week the right ankle was affected similarly. On medical advice the patient tried Balneotherapy, after which the left ankle was affected and the girl began to feel pains in the fingers, especially the middle fingers which became very swollen. On taking hot sulphur baths she suffered an intense articular irritation, affecting the elbows,

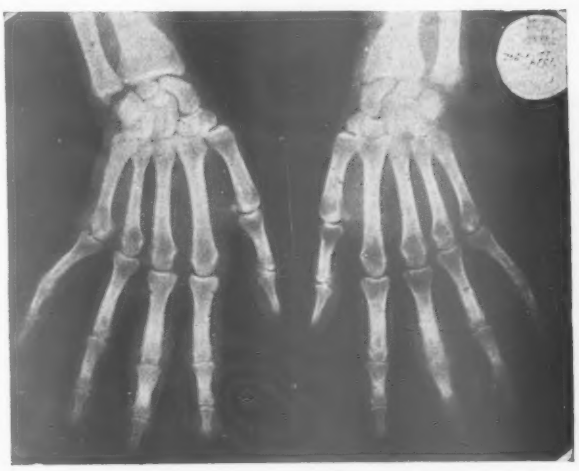

FIG. 1.—Rheumatoid arthritis before treatment (January, 1942): Decalcification most marked in the epiphyses. Fusiform peri-articular swelling of the middle fingers. Narrowing of the articular space of the proximal interphalangeal joint on the left middle finger where there is a punched-out area. Complete obliteration of the proximal interphalangeal joint of the right middle finger.

* A paper read before the Section of Radiology of the *Associação Paulista de Medicina* on Aug. 22, 1944, and also at the First *Paulista* Congress of Rheumatology and the Second Medical Congress of the State of São Paulo, Brazil (Mar. 1 to 7, 1945).

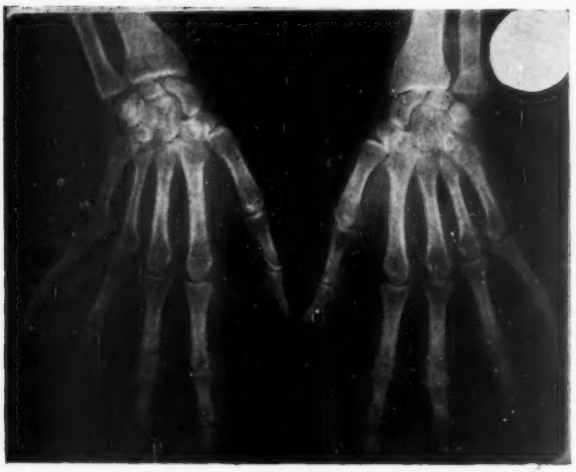

FIG. 2.—Intermediate period (July, 1942): Slight recalcification with the re-appearance of the joint spaces of the proximal interphalangeal articulations of the middle fingers. Decrease of the swelling of the soft periarticular tissues.

shoulders, jaws, and some chondro-costal joints. Concomitantly there was further loss of weight of about 6 kg. Two months ago the patient had her tonsils removed and seven teeth extracted without any effect upon the arthritis.

Interrogation.—Nervousness, indisposition for work, adynamia and accentuated psychic depression. Previous weight: 66·5 kg. The patient had never suffered from rheumatic disease previously. The hereditary antecedents were negative so far as rheumatism is concerned.

General Physical Examination.—Asthenic girl in bad general state, with haggard appearance. Good skeletal constitution, panniculus adiposus scanty, poorly developed musculature with a very diminished tonus. Cold extremities. Weight, 55 kg.; height, 1·64 m.

Special Physical Examination.—Discoloured mucosae. Teeth in bad condition and showing several extractions. Slight systolic murmur audible at the mitral area; nothing else worthy of note in the cardio-vascular system. Blood pressure, 114/80 mm. Hg.

Articular Examination.—Hands and fingers: Active flexion of the fingers had become very difficult owing to the severe pain it caused. Marked swelling at the proximal interphalangeal joints of the middle and ring fingers, especially the middle fingers which presented a characteristic fusiform aspect. Atrophy and immobility of the terminal interphalangeal joints. Lateral pressure on the joints elicited tenderness. Congenital deformity of the little fingers and pathological deformity of the right ring finger, with lesser evidence in other fingers. Skin cold and clammy.

Wrists: Diminished function, chiefly in the right where considerable swelling was noted.

Shoulders: movement causes pain.

Temporo-mandibular: Reduction of motility owing to pain and functional disability.

Sterno-clavicular and chondro-costal joints: painful at rest or on moving the arms.

Knees and ankles: Increase in size, painful at rest and the pain is aggravated by pressure or movement.

Walking: impossible, owing to pain in the weight-bearing joints. Could only walk when supported by two persons.

Laboratory Findings.—The changes in the blood count, etc., are shown in Table 1.

Radiological Findings.—Decalcification of the carpal bones, metacarpals, and phalanges, most marked at the epiphyses. Narrowing of the articular space of the proximal interphalangeal joint of the left middle finger, where one observed a punched-out area in the internal margin of the proximal extremity of the middle phalanx and entire obliteration of the joint space of the same

TABLE 1

EVOLUTION OF THE BLOOD PICTURE

Initial results (February, 1942)	Intermediate results (July, 1942)	Final results (December, 1942)
Red cell count 4,040,000	4,750,000	4,880,000
White cell count 5,950	5,050	5,350
Haemoglobin (8·4 gm. per 100 c.cm.) 50·6%	(14·4 gm. per 100 c.cm.) 86·4%	(15·1 gm. per 100 c.cm.) 90·6%
Colour index .. .. .. 0·62	0·9	0·92
Neutrophils myelocytes .. 0·0%	0·0%	0·0%
,, metamyelocytes .. 0·5%	0·0%	0·5%
,, non-filamented .. 6·5%	7·0%	4·0%
,, segmented .. .. 52·0%	58·0%	58·5%
Eosinophils .. .. .. 1·0%	8·0%	5·0%
Basophils .. .. .. 0·5%	0·0%	0·0%
Lymphocytes .. .. .. 16·0%	18·0%	21·0%
Monocytes .. .. .. 22·0%	6·0%	3·5%
Erythrocytes: Evident hypochromia; no evident alterations of the size and form; absence of immature cells of the normal or embryonic series, and also absence of nuclear remains.	No alterations worthy of note.	Slight anisocytosis.
Leucocytes: Numerous, with toxic granulations and nuclear pyknosis.	Absence of nucleo-cytoplasmic alterations.	Numerous neutrophils with nucleo-cytoplasmic alterations more or less intense and in particular with heavy toxic granulations.
Sedimentation rate (Westergren):		
1st hour .. .. .. 90 mm.	1st hour .. .. 3 mm.	1st hour .. .. 7 mm.
2nd hour .. .. .. 111 mm.	2nd hour .. .. 8 mm.	2nd hour .. .. 22 mm.

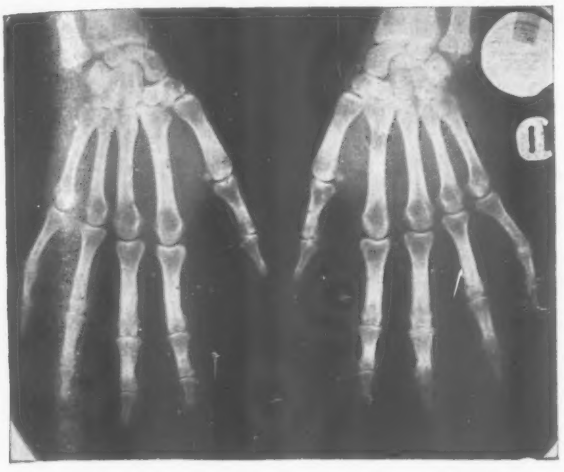

FIG. 3.—After treatment (December, 1942) Normal: appearance. Total recalcification. Articular space with their physiological dimensions. The only remaining lesion is the punched-out area.

finger and of the same articulation of the right hand. Fusiform periarticular swelling of the middle fingers; soft tissue swelling of the wrists; widening at the joint space of radius and ulna (Figs. 1, 4, and 6).

Clinical Course

This girl began her treatment at the end of February 1942, and during the two following months there was an acceleration of the disease with aggravation of all the symptoms. In April the first improvement began to appear, characterized by an increase of appetite and consequent increase in weight, progressive diminution of joint pains, less marked psychical depression, better disposition toward domestic activities, and freer movement of the fingers and wrists. These improvements increased gradually and progressively; in July the pains in the knees and ankles had disappeared, so that it was once again possible for the patient to walk. The body weight went up to 62·8 kg. At this stage there remained only vestiges of the fusiform swelling of the fingers. The psychical condition became normal and the capacity for physical activity improved by about 60%.

During the following months the organic and articular symptoms improved and the pains in the temporomandibular and hand joints began to disappear little by little, so that in December of the same year articular function and stability, and normal weight had been regained. That is, there was a complete disappearance of the pain, the haematological and radiological pictures became normal, while the weight reached 66·2 kg. and increased to 66·5 kg. by the middle of January, 1943. There was a complete restoration of physical resistance with return to a normal mode of life, the patient being discharged as clinically "cured." Table 2 shows the changes in the joints.

TABLE 2

JOINT MEASUREMENTS IN CENTIMETRES, BEFORE AND AFTER TREATMENT

Articulation	February, 1943	December, 1943
Right wrist	19 cm.	16 cm.
Left wrist	18 ,,	16 ,,
Right elbow	24 ,,	24 ,,
Left elbow	24 ,,	24 ,,
Right ankle	28·7 ,,	26·5 ,,
Left ankle	28·5 ,,	26·5 ,,
Right knee	39·7 ,,	37·5 ,,
Left knee	39·5 ,,	37·5 ,,

Radiological Course

A second radiograph taken in July, 1942, during the intermediate period of treatment, showed slight recalcification in all of the bones (Fig. 2), with the reappearance of the joint spaces of the proximal interphalangeal articulations of the middle fingers, while at the same time a decrease of the inflammatory process of the soft peri-articular tissues was noted. Films taken in December of the same year showed a normal appearance with complete recalcification. The articular spaces are seen to have regained their normal dimensions (Figs. 3, 5 and 7). The only evidence of the process which remained was the punched-out area, an atrophic lesion which we suppose to be irreversible (Fig. 7).

Discussion

The progress of the general, haematological, and articular states was parallel to that of the radiological findings, as is shown in the tables. The rarity of the return to normal of an articular space, such as took place in this case, has its explanation in the biochemistry of the cartilage. Cartilage consists of a tissue destitute of blood vessels and lymphatics, and nourished by osmosis from the synovial fluid and the subchondral vessels. Its metabolism is small and its capacity for repair and restoration insignificant, so that it is the most

FIG. 4.—Right middle finger before treatment.

FIG. 5.—Right middle finger after treatment.

FIG. 6.—Left middle finger before treatment.

FIG. 7.—Left middle finger after treatment.

vulnerable part of the articulation. As the necessity for nutrition of the cartilage is small, it is not vascularized, which is why its capacity for regeneration is nearly nil, so that small lesions in its continuity take months to repair.

In rheumatoid arthritis, the diminution of the joint space is proportional to the wear and tear of the cartilage. In the case of our patient the proximal interphalangeal joint of the middle finger of the right hand had practically disappeared, which permits us to suppose that the cartilaginous affection had been intense. However, this fact did not prevent the *restitutio ad integrum* of the articular state. Besides this organic repair, which does not appear to have been observed before, and the recalcification which took place, an equally uncommon feature is the parallelism of the clinical and radiological improvement.

More than two years have passed since the patient was discharged and the clinical, haematological and radiological condition remains normal. Nevertheless we shall have to wait for at least another year before we may definitely regard cure as established.

REFERENCE

Morrison, S. L., and Kuhns, J. G. (1936). *Amer. J. Roentgenol.*, 35, 645.

RHEUMATOID ARTHRITIS

REVIEW

BY

G. D. KERSLEY

Since 1939 there has been no epoch-making discovery in relation to rheumatoid arthritis, but, as Davidson (1944) remarks, any tendency to discourage the attainment of better facilities for treatment and research, because we do not yet know the specific cause of the disease, is as ridiculous as it would be disastrous. During the war years much has, however, been written on the subject of rheumatoid arthritis and our ideas have crystallized in several directions.

Aetiology

As stated above, the cause of rheumatoid arthritis is not known, but Davidson (1945) voices British opinion in stating that " suggestive features favour the view that infections play some aetiologic role," but that most evidence points to the fact " that it is due to the abnormal immunological reaction of the host to infection " rather than the response to a specific infection. Levinthal (1939) comes to the conclusion that the essential factor is an abnormal immune body response, while both Angevine and Fraser (1942), in separate series of blood and synovial fluid cultures, find no evidence to support a specific infective aetiology. Slater (1943) assesses the case records of 388 cases and comes to the conclusion that fatigue and emotional crises are of great importance, but that the effect of heredity, the endocrine system, pregnancy, the menopause, body build, vitamins, and diet are not proven causative factors. He found that 70% of the cases were women and that the average age of onset was 40.

Pemberton (1945) discusses rheumatoid arthritis as a " mesodermatosis " and brings out the possible interrelationship between the arthritides and the arthroses. He also mentions the importance of the psychosomatic element (Halliday, 1941), and reminds us that an analysis of cases arising after the 1914–1918 war showed an exposure factor in 60%, but no evidence to back up focal infection as of importance.

Selye (1944) produced a polyarthritis with, in some cases, lesions very similar to Aschoff's nodes and polyarteritis nodosa, by administering to rats desoxycorticosterone in large doses with extra sodium chloride, but this work has not yet been confirmed and the dosage used was extremely high.

Snyder (1943) found benefit in rheumatoid arthritis and ankylosing spondylitis from massive doses of vitamin D: in 32 cases the results were classified as 5, very good; 2, good; and 18, fair. The dosage used was very high, and, again, these results, so far, are unconfirmed.

Gardner (1945), following up Hench's work on jaundice and rheumatoid arthritis, found that remissions occurred in 25 out of 32 cases and lasted on an average for 42 days.

The relation of psoriasis to rheumatoid arthritis has been reviewed (Bauer, 1941) and its incidence given as 2·7% among rheumatoids and only 0·7% in controls. Characteristics are that it usually affects the nails, the bony destruction in the joints is very rapid, and either the arthritis or the psoriasis may make its appearance first.

Morbid Anatomy

Whereas, in this country, there is great scepticism over the interrelation between rheumatoid arthritis and rheumatic fever, in America the post-mortem findings in rheumatoid arthritis of cardiac lesions resembling those found in rheumatism in a high percentage of cases has revived interest in this possibility. Young and Schwedel (1944) found such lesions in 24 out of 38 cases; Bayles (1943) in 6 of 23 cases, and Rosenberg and Baggenstoss (1943) in 16 out of 30. The interpretation of these results depends on what is considered to be pathognomonic of an Aschoff node. The same question has been raised over the subcutaneous nodules found in both syndromes; many think them of the same pathology, though those in rheumatoid arthritis are larger and come and go more slowly (Dawson, 1933), but Collins (1937) considers them to be a non-specific connective tissue reaction, which can be produced by a number of stimuli such as traumatic tenosynovitis, vitamin C deficiency, and granuloma annulare. The rheumatoid arthritis nodule can, however, usually be distinguished under the microscope from that obtained from a rheumatic fever case. This view is held both by Collins (1939) and Bennett (1943). Nodules just visible to the naked eye (0·14–0·2 mm. diameter) have been described in the perineurium of the peripheral nerves in 7 of 8 cases of rheumatoid arthritis examined post mortem (Leichtentritt, 1943), but in none of 100 controls. It is suggested that these lesions may be responsible for some of the neuritic pains and trophic changes,

wasting and spasm, so frequently found in this condition. Similar nodules, some visible only under the microscope, were discovered by Freund in all of 14 muscle biopsies from rheumatoid subjects, but in none of a large number of controls.

A further paper that may well help to revolutionize our ideas on pathology in Rheumatoid Arthritis has just been published by Steiner, Freund, Leichtentritt and Maun. They confirm the nodular inflammatory re-action around many peripheral nerves and also some of the small arteries to the muscles; they have now found the perineuritic lesions in 8 out of 10 cases at post-mortem examination. Moreover, they describe in detail " polymyositic nodules " found in all of nine cases examined, seven by biopsy and two at post-mortem, and in 9 out of 10 small samples taken from various muscles. In view of this, biopsy of muscle may become an important diagnostic criterion in atypical cases. The authors consider the primary tissue change to be in the endo- and peri-mysium with secondary degeneration in the muscle fibres. Degeneration of nervous tissue was not observed. The nodules in the connective tissue between the fibres varied in size from small collections of cells, seen only under the microscope, to those easily visible to the naked eye in sections of tissue. They were round, oval or spindle shaped and sometimes tapered off, infiltrating the planes of the endomysium. They consisted of collections of lymphocytes and plasma cells, with also a few mast cells, while around the periphery of the larger nodules were collections of epitheloid cells. An increase in collagenous connective tissue characterized by its lack of reticular network was also found. These changes were present in both early and late cases—onset 4 months to 19 years before examination—in apparently " burnt out " cases and in those treated or untreated with gold, but in none of 196 control specimens. In addition to these characteristic changes, in many there were signs of muscle degeneration, commencing with an abnormal staining re-action, " invasion " of the contractile substance of fibres by nuclei and vacuolization, irregularity of contour, loss of striation and finally shrinkage of the fibres themselves. This work demonstrates the wide-spread nature of the pathology of Rheumatoid Arthritis and histological evidence of activity during clinical quiescence. The lesions seen were quite distinct from any described in fibrositis and appear to be specific to Rheumatoid Arthritis.

Felty's syndrome of enlargement of the spleen, leucopenia, and pigmentation was not supported as a distinct entity after review of 15 cases by Hatch (1945), and the operation of splenectomy advised by Steinberg (1942) was discredited by this writer. Bach (1940) previously had reported improvement in two of three cases thus operated on.

Treatment

The use both of sulphonamides, except at the time of removal of septic foci, and penicillin (Boland *et al.*, 1944 and 1945) has been most disappointing. Likewise the bulk of the medical profession, both here and in the U.S.A., is becoming very sceptical of the value of vaccines except in specially selected cases.

The value of rest and general treatment of the patient as a whole is becoming better recognized in all critical reviews.

The correction of deformity by the use of serial plasters as advocated originally by Swaim, Kindersley (1935), and others, is now accepted both here and in the U.S.A. as the best method, capsulotomy also being employed if necessary (Freyberg, 1942; Kuhns, 1943).

Ideas on the value and dosage of aurotherapy have been modified a great deal. While for some time it has been much used for selected cases in this country, it has been regarded with suspicion, until recently, in America. Even in 1941 Bauer stated that of 30 cases of rheumatoid arthritis only 4 were improved following its administration. Comroe (1945), however, sums up the present American view, supported by all observers in this country, that gold is of definite value in active cases of the disease that are failing to react to rest and other rational, general and local treatment. Fraser (1945), working with a grant from the Empire Rheumatism Council, carried out a carefully controlled investigation on 103 cases. Fifty-seven received myocrisin (sodium aurothiomalate) and 46 a control injection.

Eighty-two per cent. of those receiving gold were improved and only 45% of the controls. The dosage used was on an average: 0·01 gm. × 1, 0·02 gm. × 2, 0·05 gm. × 1, 0·1 gm. × 9. Total: 1 gramme. Where necessary, a second course of injections was given after a lapse of three months. Slight toxic reactions occurred in 75%, but in none were they alarming. In 7 cases the treatment had, however, to be abandoned. The reactions were: general, 4; skin, 37 (2 severe); albuminuria, 30 (5 severe); stomatitis, 7; colitis, 1; agranulocytosis, none. Comroe advises a still smaller dosage: 0·005 gm. × 4, 0·01 gm. × 2, 0·025 gm. × 24. Total: 0·5 gramme; the course to be repeated in eight weeks if there was benefit from the first series. By using this very small dosage he considers that the results are equally good and that less toxic reactions are produced. He finds reduction in pain and swelling and increase in appetite and weight usually begins in one to three months after starting the injections. He points out that, if one injection of 0·1 gm. is given, only 20% is excreted in a week and that gold may be found in the urine ten months after completion of a course, the liver, kidney, spleen, and skin, in particular, acting as depots. Goldie (1939) carefully correlated the sedimentation rate, during aurotherapy, in 400 cases. He found that the initial sedimentation rate had no bearing on the prognosis, but the clinical improvement and fall in the sedimentation rate during treatment usually coincided. If there was no fall in the sedimentation rate during the first course a second was also unlikely to produce one.

With regard to the best preparation of gold to be used, Sabin (1941) found that the effectiveness of the gold salt varied with its gold content. Comroe advises the crystalline salts rather than the colloidal ones as being more effective, though more toxic, and Freyberg (1942) advocates calcium aurothiomalate (auro-calcium) as slightly less toxic than the sodium salt (myocrisin).

To sum up—aurotherapy has come to stay till something better is discovered. Very small dosage is needed, and the crystalline organic calcium salt probably is the least toxic of the really effective preparations available.

References

Angevine, D. M. *et al.* (1942). *Ann. Rheum. Dis.*, 3, 101.
Bach, F., and Savage, O. (1940). *Ibid.*, 2, 47.
Bauer, W. *et al.* (1941). *Trans. Ass. Amer. Phys.*, 56, 349.
Bayles, T. B. (1943). *Amer. J. med. Sc.*, 205, 42.
Bennett, G. A. (1943). *Ann. intern. Med.*, 19, 111.
Boland, E. W., Headley, N. E., and Hench, P. S. (1944). *Proc. Mayo Clin.*, 19, 505. (1945). *Ann. Rheum. Dis.*, 4, 76.
Collins, D. H. (1937). *J. Path. Bact.*, 35, 97. (1939). *Ann. Rheum. Dis.*, 1, 38.
Comroe, B. I. (1945). *J. Amer. Ass.*, 128, 848.
Copeman, W. S. C. (1936). *Rep. Rheum. Dis. London*, 2, 24.
Davidson, L. S. P. (1943), *Glasgow Med. Jour.*, 140.
Dawson, M. H. (1933). *J. exp. Med.*, 57, 845.
Fraser, T. N. (1945). *Ann. Rheum. Dis.*, 4, 71. (1942). *Ibid.*, 3, 181.
Freund, H. A., *et al.* (1942). *Amer. J. Path.*, 18, 865. (1945). *Science*, 101, 202.
Freyberg, R. H., *et al.* (1942). *Proc. Mayo Clin.*, 17, 534. (1942). *Ann. Rheum. Dis.*, 3, 77.
Gardner, F., *et al.* (1945). *Brit. Med. J.*, 2, 677.
Goldie, W. (1939). *Ann. Rheum. Dis.*, 1, 319.
Halliday, J. L. (1941). *Ann. inten. Med.*, 15, 666.
Hatch, F. N. (1945). *Ibid.*, 23, 201.
Hench, P. S., (1938). *A survey of Chronic Rheumatic Diseases*, 35. London
Kindersley, C. E. (1935). *Proc. roy. Soc. Med.*, 29, 237.
Kuhns, J. G. (1943). *Ann. inten. Med.*, 10, 131.
Leichtentritt, B. (1943). *Ibid.*, 19, 116.
Levinthal, W. (1939). *Ann. Rheum. Dis.*, 1, 67.
Pemberton, R. (1945). *Amer. J. Med. Sci.*, 209, 364.
Review of Amer. and Eng. Literature. 1940. Hench, P. S. *et al.* (1941). *Ann. inten. Med.*, 15, 1002.
Rosenberg, E. F., Baggenstoss, A. H., Hench, P. S. (1943). *Ibid.*, 19, 116.
Sabin, A. B. (1941). *Bact. Rev.*, 5, 1.
Selye, H., *et al.* (1944). *J. Amer. med. Ass.*, 124, 201.
Slater, J. G. (1942). *Ann. Rheum. Dis.*, 3, 195.
Snyder, R. G., *et al.* (1943). *Ann. inten. Med.*, 19, 125.
Steinberg, C. L. (1942). *Ibid.*, 372.
Steiner, G., Freund, H. A., Leichtentritt, B., and Maun, M. E. *Amer. J. Path.*, 1946, 22, 103.
Young, D., and Schwedel, J. B. (1944). *Amer. Heart J.*, 28, 1.

THE HEBERDEN SOCIETY

The Heberden Society for the advancement of the study of the Rheumatic Diseases was founded in 1936, contemporaneously with the Empire Rheumatism Council but with a more specialized aim: the intensive culture of clinical knowledge among medical practitioners in this group of diseases. Its growth suffered, as did so much of humane activity, through the outbreak of World War II. Now that the era of peace has opened the Society has returned to its task. Towards the end of 1945 the Annual Dinner was revived and the address of the President (Dr. C. W. Buckley) described the Society's past, and outlined its future, activities.

THE PRESIDENT'S ADDRESS

The Heberden Society now enters upon a new chapter in its history, a chapter which we hope will be associated with advances of importance in the study of those common diseases grouped under the general term " rheumatic "—diseases so prevalent that familiarity has bred contempt, but which have been well described by Lord Horder as the most serious enemy of home happiness and industrial efficiency. They have appeared frequently to be regarded as unworthy of the attention of the professors of medicine interested only in higher things. In consequence many newly graduated doctors have embarked upon practice with little or no knowledge of the diseases which will probably form about 10% of their work. A few names, however, stand out in the history of medicine associated with rheumatism and notable among these were the Heberdens, father and son, a name we are proud to associate with this society, a happy suggestion for which credit goes to Dr. Ray. Did time permit one might mention many others such as the Garrods, again father and son. To Archibald Garrod belongs much of the credit for advancing the study of chronic rheumatism and laying the foundations for the enhanced work on the subject which has marked the last quarter of a century.

The appointment by the British Medical Association of a committee (1931) to report on chronic rheumatic disease was an important indication of awakening interest. Three years later a committee was appointed by the Royal College of Physicians with a similar object and the publication of their " Reports " was the forerunner of the *Annals of the Rheumatic Diseases*, which may now be regarded as the journal of this Society.

Empire Rheumatism Council

The formation of the Empire Rheumatism Council (1936) followed and marked an important epoch in the history of the campaign against rheumatism. It owes its inception largely to the vision and energy of Lord Horder, and brought together those who were conscious of the importance of the subject. The value of its propaganda in arousing interest and stimulating public-spirited men and women to advance its objects by financial support, and in many other ways, cannot be over-estimated. The publication by the Council of *Rheumatism—a Plan for National Action*, from the pen of Lord Horder, attracted wide attention and is approaching its tenth thousand—clear evidence of the awakening of public interest. The war seriously interfered with the Council's activities but its work has been carried on in spite of enormous difficulties, which have been described in the successive Annual Reports. Apart from its propaganda work much has been done in directing and subsidizing research. This work was also interfered with by the war but not interrupted entirely. Though the campaign may in some measure be carried on in future as part of the proposed National Health Service, there will still be scope for private initiative and the direction which can be exercised by the Council will be important.

About the same time as the formation of the Empire Rheumatism Council, the medical staff of the Red Cross Clinic, with others immediately interested in the work of the Clinic, formed a Society for the discussion of the clinical and pathological aspects of chronic rheumatic disease and adopted the name of the great clinician who was among the earliest to attempt to study those crippling and painful joint conditions grouped under the term " arthritis," and to disentangle from them that form of osteo-arthritis now so familiar to us as " Heberden's nodes."

The Society had begun to attract attention and to gather members from outside the original sphere of its activities when the war broke out, and it seemed possible that, like so many other societies of the kind, it might pass into oblivion. However, though it ceased to meet, the spirit which led to its formation was still alive among its members and important work has been done during the years of the war, stimulated by the incidence of rheumatism in the Forces and the opportunities presented to keen students of observing the effects of climate, physical strain, and other aetiological factors. Notable among the researches carried out by members of this society has been the work of Copeman and his colleagues on fibrositis, that protean form of rheumatism which Gowers described and named and Stockman studied. In spite of the work of these pioneers and of others who have carried out important studies, doubts were for long expressed, particularly in America, as to whether fibrositis was a pathological entity, but these doubts are no longer heard thanks to the work of British physicians.

With the end of the war the time seemed to be appropriate to widen the scope of the Society and to link together all who were interested in the branch of medicine with which it was concerned. The idea was welcomed and the Heberden Society has now renewed its youth and will, we hope, soon become one of the most important medical societies of its kind.

The rejuvenation of the Society has been marked by its affiliation with the Empire Rheumatism Council, a definite gain to the Society and we hope to the Council also. One outcome of this is that the *Annals of the Rheumatic Diseases*, the only journal devoted to rheumatism which has continued to appear regularly throughout the war, and which is now published as a quarterly journal by the B.M.A., will report the proceedings of the Society and be circulated to the members.

Great possibilities lie before us and much scope for important achievements. Research workers often seem to plough a lonely furrow and may fail to gain recognition on that account unless some striking result is achieved, based it may be on the work of others who fail to gain the credit they have deserved. On the other hand the value of team work may be overlooked. It offers no glory and, under present conditions, inadequate rewards. Many a newly fledged graduate with an inquiring mind and a bent towards research has been obliged to forego a career for which he may have been exceptionally fitted in order to earn a living in more lucrative forms of practice. General practice does, how-

ever, provide an unrivalled field for clinical observation on hereditary, familial, social, occupational, climatic, and meteorological influences, and I hope this society will endeavour to encourage practitioners to study these problems and submit their results for discussion or publication. The stimulus of discussion with other workers in the same field will thus be forthcoming; direction and guidance may be obtained and zest added to the work. It should not be forgotten that negative results may be important, the ground must be cleared of rubbish and of the weeds of superstition and fallacious beliefs before the foundations of a more worthy edifice can be established. A new type of meeting might help, not one with set papers but an informal gathering for discussion upon common forms of rheumatism, illustrated it might be by clinical cases. Popular beliefs and heresies might also prove to be worthy of examination; it sometimes happens that such beliefs are not without a basis of experience. It is well to remember the saying of Francis Bacon, which appears on Erichsen's title page as a guide to young surgeons, " They be the best Chirurgeons which, being learned, incline to the traditions of experience or, being empirics, incline to the methods of learning."

The Clinical Approach

The Heberden society, following the practice of the physician whose name it bears, has as its primary object the study of the clinical aspects of rheumatic disease which includes aetiology, pathology, and symptoms. Treatment cannot of course be ignored, and it must obviously be the duty of all clinicians to study treatment in its various forms and to endeavour to correlate it with pathology. I question whether any group of diseases has suffered more from methods of treatment devised without any consideration of the underlying pathology responsible for the symptoms presented. The label, often provided by the patient, has been the sole basis for the treatment adopted, whether the advice on that has been forthcoming from the family doctor, the local druggist, the fellow-traveller, or the solicitous neighbour. The patient tells you that he has rheumatism and often displays impatience if asked to recount his symptoms. Why should you need that when he has told you what is the matter with him? This attitude is sometimes due to his doctor who, in a busy general practice, finds it difficult to listen to a tedious description, in the course of which, however, the patient may quite unwittingly reveal some essential factor. I recently had an instance of the danger of dismissing a case in this way. I had seen an elderly lady and, after examination and radiography, had arrived at a diagnosis of intercostal neuralgia due to spinal osteoporosis of senile type. When the patient saw her family doctor he read my letter and forthwith dismissed the matter with the words, " only another form of rheumatism."

The proportion of cases that have not at some stage received *mist. sodae sal.* is small, and perhaps smaller still the number who have not dosed themselves with some form of salts, or other " cures." Most of them are harmless save in one respect and that a grave one: they are often responsible for postponement of proper examination and adequate treatment until irreparable damage has been done.

There are few cases in which properly directed physiotherapy is not an essential part of the treatment of chronic rheumatism, but it must not be forgotten that a wide acquaintance with physical methods of treatment does not make a specialist in the rheumatic diseases. The relief of symptoms by heat, massage, or other measures does not cover the whole field. There are societies concerned with physical medicine which must concern themselves with rheumatism as one of their chief spheres of activity. The Heberden society does not aim to trespass on their ground and for that reason the clinical aspect will always be its primary object. Even so, light from any quarter will be welcomed. It was said in the preface of a book on rheumatism published shortly before the war, " obscurities will remain until the biochemist and the biophysicist are enticed and encouraged to join in the work." We shall welcome their help. The *Annals* will always publish matter of interest and it is hoped that in future it will include as a regular feature abstracts and reviews of all important work on our subject from all parts of the world. That would add greatly to its value. I look forward to its attaining a wide circulation among general practitioners, and bringing to them in readable form the most recent work in rheumatology as well as drawing attention to the work of this Society in the campaign against rheumatic disease.

It has been though expedient to limit the numbers of members of the Society to one hundred, at least for the present. An essential qualification for membership is an active interest in the study of rheumatism, acute and chronic. It is not to be expected that original work will be forthcoming from every member, nor perhaps would that be desirable, but it is hoped that members will attend the meetings so far as may be possible and take part in the discussions. Possibly, opportunities will arise to invite members to make systematic observations on causation and treatment, and thus to combine in practical research. Suggestions for increasing the usefulness of the Society will always be welcome. Although the headquarters must be in London it is hoped that provincial meetings may be arranged from time to time and representation on the Executive will provide for a proportion of members from outside the metropolis.

An account of the activities of the Heberden society would be incomplete without reference to the Heberden Medal, which is awarded from time to time for distinguished original work in rheumatology; credit for establishing this is due to Dr. Heald. It is a distinction to be coveted as a mark of valuable contributions to our knowledge and has already been bestowed on distinguished workers in the subject. Furthermore, it is a beautiful example of the art of the medallist.

SCIENTIFIC MEETINGS

The first scientific meeting was held at the Royal Free Hospital on Nov. 2, 1945, and members (with, in addition, a number of post-graduates attending a course organized by the Empire Rheumatism Council) were hospitably entertained by the Matron. Exhibits at this meeting were:

(*a*) Relief map modelling as a form of occupational therapy.
(*b*) Photographic studies of the hand in arthritis.
(*c*) " Rest splints " in perspex.
(*d*) A captured German " metal-seeking " apparatus.
(*e*) Mobile physiotherapy cabinet.

Members then attended a series of lecture-demonstrations on recent advances in physical methods, arranged by Dr. C. B. Heald. The majority of these demonstrations were by kind permission of the Air Ministry. F/Lt. B. C. Elliott described and demonstrated—

1. A new short-wave diathermy apparatus which, provided a wave-length was allocated for medical use, could be used without screening. The difference in interference with wireless reception between this and the commercial short-wave apparatus at present in use was ably and strikingly demonstrated.
2. An improved apparatus for the galvanic treatment of denervated muscles. By this apparatus, called the " balanced pulse generator," ionization is eliminated and strong, painless contractions can be obtained.
3. An improved ultra-violet light efficiency tester.

Dr. Graham Weddell demonstrated possible uses of the electromyograph in clinical medicine, and its value

in the investigation of the character of so-called " fibrositic lesions."

Sister F. L. Greemhill gave a most able and helpful demonstration of the Guthrie-Smith suspension apparatus and its use in most forms of remedial exercises.

The President expressed, on behalf of the Society, grateful thanks to all who had contributed to the success of a carefu'ly organized series of important demonstrations.

The secord Scientific Meeting was held at the Middlesex Hospital, Nov. 3, 1945, by kind permission of the Secretary and Matron. Professor B. Windeyer read a paper on the treatment of ankylosing spondylitis by x rays, reviewing his own results over a period of about ten years. The paper was followed by a demonstration of some twenty patients suffering from the disease who were under treatment.

Business Meeting

At the business meeting, Nov. 2, 1945, the following were nominated by the Executive Committee and were unanimously elected as Ordinary Members:

Professor C. Bruce-Perry
Dr. E. L. G. Bywaters
Mr. N. Capener, F.R.C.S.
Dr. Frank Clayton
Dr. F. S. Cooksey
Dr. E. C. Cosgrove
Dr. I. Easton
Dr. Horace Evans
Dr. G. J. Griffiths
Dr. L. C. Hill
Dr. G. L. Kerr-Pringle
Dr. J. Lovelock
Mr. A. M. A. Moore, F.R.C.S.
Dr. J. W. T. Patterson
Lt.-Col. T. G. Reah
Dr. Oswald Savage
Dr. R. E. Tunbridge
Dr. W. Yeoman
Dr. A. Hutton Wilson

It was agreed—

1. That provision should be made for Honorary Membership for distinguished members of the profession who could be of service to the Society, but who are not engaged in practice.

2. That invitations to accept honorary membership should be sent to: (*a*) the holder of the office of President of the Royal College of Physicians; (*b*) the holder of the office of President of the Royal College of Physicians of Edinburgh; (*c*) the Chief Medical Officer of the Ministry of Health; (*d*) the Chairman of Council, Empire Rheumatism Council; and (*e*) the Director-General of the E.M.S.

EMPIRE RHEUMATISM COUNCIL

Minutes of the Annual Meeting held on Dec. 13, 1945, *at* 11, *Chandos Street, London, W.*1, *Lord Horder in the Chair*

Apologies for unavoidable absence were received from: Dr. Bailey, Mr. B. T. Clegg, Mr. Norman Capener, Lord Gretton, Colonel Hilder, Dr. Donald Hunter, Professor Humphries, Mr. C. G. Izard, Sir Alexander Maclean, Mr. T. W. Robinson, Mr. Wood Smith.

1. Minutes of the previous meeting (held in 1938) were read and confirmed.

2. The Annual Report by the Chairman, Lord Horder, which had been circulated was received. On the motion of Sir Walter Kinnear, seconded by Air Vice-Marshal Don, it was resolved: "That the Report be adopted and that the proposals for future action embodied therein are approved in principle."

3. The Finance Report, by the Finance Committee, which had been circulated was received. On the motion of Sir Walter Kinnear, seconded by Dr. C. W. Buckley, the Report was adopted.

4. The meeting proceeded to the election of officers and Committees for 1946. The following were elected:

Chairman: Rt. Hon. Lord Horder, G.C.V.O., F.R.C.P.

Executive Committee: Rt. Hon. Lord Horder, G.C.V.O., F.R.C.P. (*ex officio*); Dr. W. S. C. Copeman, O.B.E., F.R.C.P. (*ex officio*); Air Vice-Marshal Don, O.B.E.; A. G. Timbrell Fisher, M.C., F.R.C.S.; Rt. Hon. Lord Gretton, P.C.; Dr. F. D. Howitt, C.V.O., F.R.C.P.; C. G. Izard; Sir Walter Kinnear, K.B.E.; E. R. A. Merewether, M.D., F.R.S.E.; J. W. T. Patterson, F.R.C.P.E.; T. W. Robinson, A.C.A.; Dr. W. S. Tegner, M.R.C.P.

Finance Committee: Sir Walter Kinnear, K.B.E.; C. G. Izard; T. W. Robinson, A.C.A.

Scientific Advisory Committee: Sir Adolphe Abrahams, O.B.E., F.R.C.P.; C. W. Buckley, F.R.C.P.; Norman Capener, F.R.C.S.; Professor H. Cohen, F.R.C.P.; Professor L. S. P. Davidson, F.R.C.P.E., F.R.S.E.; A. G. Timbrell Fisher, M.C., F.R.C.S.; E. Fletcher, M.R.C.P.; F. D. Howitt, C.V.O., F.R.C.P.; G. Kersley, F.R.C.P.; E. R. A. Merewether, M.D., F.R.S.E.; J. W. T. Patterson, F.R.C.P.E.; B. Schlesinger, F.R.C.P.; W. S. Tegner, M.R.C.P.; E. T. Conybeare, F.R.C.P. (liaison with the Ministry of Health), (The Chairman and the Hon. Medical Secretary are *ex officio* members.)

Honorary Medical Secretary: Dr. W. S. C. Copeman, O.B.E., F.R.C.P.

Organizing Secretary: Sir Frank Fox, O.B.E.

Lord Horder noted for the information of members that it was proposed that the Chairman of the Executive Committee, when chosen by that Committee, should become Vice-Chairman of the Council, and that a bacteriologist should be added to the Scientific Advisory Committee. These proposals were agreed unanimously.

5. On the motion of Dr. Heald (who expressed appreciation of the extremely valuable service of the War Emergency Committee) seconded by Dr. Kersley, it was resolved unanimously: "This meeting endorses the actions taken by the War Emergency Committee, as reported yearly to all members, in conducting since October 1939 the affairs of the Council: expresses its cordial thanks for their devoted service to the work of the Council; and, in relieving its members from their responsibilities, invites them to accept honorary life membership of the Council.

Votes of thanks to the Chairman, to the Honorary Auditors, and to the staff, were carried unanimously.

RHEUMATISM IN SWEDEN

There continue to be indications of the serious attention the Swedish Government is giving to the extension of the provision of treatment of rheumatism. The Committee of Rheumatological experts appointed in 1941, which in 1942 recommended the establishment of special centres in Stockholm and Upsala, is now investigating the question whether those special centres will be sufficient to meet the need and whether their work can be reinforced by the establishment of subsidiary centres. Such centres would be able to deal with the less difficult cases and with convalescent cases still requiring some medical care, but not on the same scale as that provided in the special institutions referred to in the report in our last issue.

The aim of this is to secure economy in administration. It is also proposed that the control of the five centres for rheumatic patients established by the Pensions Board should be transferred to the appropriate County Councils.